TO ANALYZE THE RESPONSE OF PLATELET TRANSFUSION IN ONCO HEMOTOLOGY PATIENTS

A THESIS SUBMITTED TO BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT (PUNJAB) IN THE PARTIAL FULFILLMENT

FOR THE AWARD OF DEGREE OF DOCTORATE OF MEDICINE IN IMMUNO HAEMATOLOGY AND BLOOD TRANSFUSION

2024

Dr. SHALINDERJEET KAUR

DEPARTMENT OF IMMUNO HAEMATOLOGY AND BLOOD TRANSFUSION

DAYANAND MEDICAL COLLEGE & HOSPITAL

LUDHIANA, PUNJAB-141001

DECLARATION BY THE CANDIDATE

I hereby declare that the thesis entitled "**TO ANALYZE THE RESPONSE OF PLATELET TRANSFUSION IN ONCO HEMOTOLOGY PATIENTS**" submitted towards partial fulfillment of the requirements for the award of **MD in** Immuno Haematology and Blood Transfusion degree to BFUHS is a compilation of original work carried out by me under the supervision **Dr. Sonia Gupta**, Associate Professor, Department of Immuno Haematology and Blood Transfusion and **Dr. Rajesh Kumar**, Professor & Head, Department of Immuno Haematology and Blood Transfusion. No part of this thesis has formed the basis for the award of any degree previously.

_____

Dr. Shalinderjeet Kaur
M.D Resident
Dept. of IHBT
DMC & Hospital,
Ludhiana

Date:

Place:

CERTIFICATE OF SUPERVISORS

This is to certify that the work incorporated in this thesis entitled "**TO ANALYZE THE RESPONSE OF PLATELET TRANSFUSION IN ONCO HEMOTOLOGY PATIENTS**" has been carried out by **Dr. Shalinderjeet Kaur** under our direct supervision. The data incorporated in this thesis is original and genuine and has been carried out by the candidate herself.

Signature of Supervisor

Dr. Sonia Gupta
Associate Professor,
Department of IHBT
DMCH, Ludhiana

Signature of Co-Supervisor

Dr. Rajesh Kumar
Professor & Head
Department of IHBT
DMCH, Ludhiana

Date:

ENDORSEMENT BY THE HEAD OF THE INSTITUTE

This is to certify that the thesis entitled "**TO ANALYZE THE RESPONSE OF PLATELET TRANSFUSION IN ONCO HEMOTOLOGY PATIENTS**" is a bonafide research work done by **Dr. Shalinderjeet Kaur** under the supervision **Dr. Sonia Gupta**, Associate Professor, Department of Immuno Haematology and Blood Transfusion and **Dr. Rajesh Kumar**, Professor & Head, Department of Immuno Haematology and Blood Transfusion in this institution.

Principal

Dr. G S Wander
Principal
DMC&H, Ludhiana

Date:

COPYRIGHT

Declaration by the Candidate

I hereby declare that the Baba Farid University of Heath Sciences, Faridkot, shall have the rights to preserve & use this thesis in print or electronic format for academic/study purpose by the research scholar/students.

Signature

Dr. Shalinderjeet Kaur
M.D Resident
Department of IHBT,
DMC & Hospital,
Ludhiana

Date:

© Baba Farid University of Health Sciences, Faridkot

Dedicated

To My

Taiya ji,

My Family

&

Teachers

ACKNOWLEDGEMENT

I thank almighty for giving me an opportunity to become a doctor and thus giving me a golden chance to serve the humanity through this noble profession. This thesis has been kept on path and been to completion with the support and encouragement of numerous persons including my family, teachers, colleagues and friends.

First and foremost, I would like to extend my sincere gratitude to my research guide **Dr. Sonia Gupta,** Associate Professor Department of IHBT, Dayanand Medical college and hospital for her guidance, help, advise, inspiration, encouragement, and continuous support, throughout my study period. Her enthusiasm, integral view on research and her mission for providing high-quality work, has made a deep impression on me. Under her guidance I successfully overcame many difficulties and obstacles.

I am extremely thankful to **Dr Rajesh Kumar**, Professor and Head of Department, IHBT, Dayanand Medical College and Hospital, Ludhiana, as his timely help, advice, instructions and suggestions have always guided me. The finest privilege in my professional career has been the opportunity to work under his inspirational guidance. . His zeal for perfection, passion, unflinching courage, and conviction has always inspired me to do more. I sincerely thank from the bottom of my heart and will be truly indebted throughout my lifetime.

I would like to give my special thanks to **Dr. Deepika Aggarwal**, Assistant Professor DMC&H and who offered me her mentorship.

At this moment of accomplishment, I am greatly indebted my **Taiya ji and my family** as a whole for their continuous support and understanding when undertaking my research and writing my thesis. Your blessings for me was what sustained me this far.

I acknowledge the people who mean a lot to me, my parents, my **Taiya Ji S. Hansa Singh**, my father **S. Gulzar Singh** and my mother **Mrs. Nirmaljit Kaur**, **Bhabhi ji**, my **brothers and Sisters** for showing faith in me and giving me liberty to choose what I desired. I salute you for the selfless love, care and sacrifice you did to shape my life.

It's my fortune to gratefully acknowledge the support of my friends and colleagues **Dr. Harleen Kaur and Dr. Jannet Mary John** for their invaluable suggestions and relentless efforts in shaping up my thesis.

My special thanks to **all my Juniors** from my bottom of heart, who always helped me in my journey.

My special friends **Aman Jaggi, Sandy, Sumit, Janvi, Simrat and Sejshi** and my loremaster **Dr Sahibjit Singh** have always extended their emotional support and sustained my courage throughout this period. Thank you all for your unwavering support and for reminding me to take breaks and have fun when I've been stressed out.

I am thankful to the **all technicians and staff** of IHBT department who helped me to conduct this study and made this uphill task possible.

A special thanks to **Mrs Namita & Mr Varinder**, Research and Development centre for their efforts.

-Dr.Shalinderjeet Kaur

ABBREVIATIONS

SDP	Single Donor Platelets
SDAP	Single Donor Apheresis Platelets
RDP	Random Donor Platelets
CCI	Corrected Count Increment
PPR	Percent Platelet Recovery
Pt	Patient
PTR	Platelet Transfusion Refractoriness
HPA	Human Platelet Antigen
DIC	Disseminated Intravascular Coagulation
HR	HOUR
AML	Acute Myeloid Leukemia
ALL	Acute Lymphocytic Leukemia
MDS	Myelodysplastic Syndrome
VOL.	Volume
BSA	Body Surface Area

ABSTRACT

Introduction: Disease and therapy related hypo proliferative thrombocytopenia is a major problem while managing the patients having onco hematological malignancies and preventive platelet transfusion has been demonstrated to be highly effective and significant in lowering the risk of bleeding in such patients. Platelet transfusion refractoriness is encountered in up to 30% of patients having hematological disease.

Aim of study: To study the response of standard and low dose of platelet transfusion in onco hematological patients.

Material and method: Study population included 100 onco hematological patients who required multiple platelet transfusions. Single donor apheresis platelets (SDAPs) was prepared by using automated cell separator and pooled platelet concentrate was prepared from whole blood donation. Apheresis product was split using sterile connecting device into two products. Pooled platelet concentrate of two units and four units were prepared using sterile connecting device.

The post transfusion counts were assessed after one hour and 24hrs of transfusion. Corrected count increment (CCI), percent platelet recovery (PPR) was calculated.

Result- 25patients (total 100) received transfusion of standard, low dose of SDP and standard, low dose of RDP in each group respectively. CCI and PPR after 1 hr with standard dose of SDP is 18.12±8.18 and 50.39 ±27.12 and with low dose is 12.53±6.81and is 26.72 ±23.70 After 24 hrs CCI and PPR with standard dose of SDP is 14.14±7.16 and 39.30 ±23.35 and with low dose is 9.15±4.07 and 18.76 ±14.09. CCI and PPR after 1 hr with standard dose of RDP is 21.36±4.57 and 59±16.63.With low dose CCI is 15.63±9.12and PPR is 37.97 ±31.01. After 24 hrs CCI and PPR with standard dose of RDP is 17.86±4.72 and 49.74±15.30.With low dose is 11.61±7.33 and is 28.23 ±24.50.

Conclusion- Post-transfusion increments were considerably greater in SDP recipients than in RDP recipients, CCI and PPR were comparable in all patient groups.

Keywords: Platelet refractoriness, onco heamatology, single donor apheresis platelet

TABLE OF CONTENTS

S. NO.	TOPIC	PAGES
I	INTRODUCTION	1-5
II	AIMS AND OBJECTIVES	6
III	REVIEW OF LITERATURE	7-17
IV	MATERIALS AND METHODS	18-19
V	OBSERVATIONS AND RESULTS	20-29
VI	DISCUSSION	30-40
VII	SUMMARY AND CONCLUSIONS	41
VIII	BIBLIOGRAPHY	42-51

APPENDICES – I

- PROFORMA
- MASTER CHART

APPENDICES – II

- APPROVAL LETTER OF THESIS PLAN
- THESIS PLAN

LIST OF TABLES

Table No.	Title	Page No.
1.	SDP & RDP Transfusion Depending On Diagnosis	23
2.	SDP & RDP Transfusions With Different Doses In Various Onco-Hematological Cases	25
3.	Platelet Counts After Transfusion of Different Doses of SDP	26
4.	Platelet Counts After Transfusion of Different Doses of RDP	28
5.	Comparing The Distribution of Various Malignancies With Other Studies	31
6.	Comparison of Platelet Counts With Respect To Different Malignancies In Various Studies	35-38
7.	Comparison of Platelet Dosages In Different Studies	39-40

LIST OF FIGURES

Fig. No.	Title	Page No.
1.	Distribution of Cases Based on Age	20
2.	Allocation of Cases Based on Sex	20
3.	Proportion of Cases Based On Diagnosis	21
4.	SDP & RDP Transfusion According to Gender	22
5.	SDP & RDP Transfusion Based on Age, Weight, Height	22
6.	SDP & RDP Transfusion Depending on Diagnosis	24

KEY TO MASTERCHART

SDP	Single Donor Platelets
SDAP	Single Donor Apheresis Platelets
RDP	Random Donor Platelets
CCI	Corrected Count Increment
PPR	Percent Platelet Recovery
Pt	Patient
HR	HOUR
AML	Acute Myeloid Leukemia
ALL	Acute Lymphocytic Leukemia
MDS	Myelodysplastic Syndrome
VOL.	Volume
BSA	Body Surface Area

BABA FARID UNIVERSITY OF HEALTH SCIENCES
Sadiq Road, Faridkot-151203 (Pb.) INDIA
Phone No. 91-1639-256253 and Fax No. 91-1639-256234
Website: www.bfuhs.ac.in, Email: bfuhspc@gmail.com
(BFUHS – UNIVERSITY LIBRARY- Coordinator APC)

11-BFUHS (LI-PC-134)24/647 Dated: July 06, 2024

Plagiarism Verification Certificate

Title of the thesis: **To Analyze The Response Of Platelet Transfusion In Oncology Haematology Patients.**

Total Page: **55 (Fifty Five only) eFSPC** **(eFile Sent for Plagiarism Check)**

Researcher: **Shalinderjeet Kaur**

Supervisor: **Dr. Sonia Gupta**

Research Centre: **Dayanand Medical College & Hospital, Ludhiana**

This is to report that the above thesis was scanned for similarity detection. Process and outcome is given below:

DID:	**2085142**	Software used:	**DRILLBIT**
Date:	**July 06, 2024**	Similarity Index:	**9% (Below 10 Percent)**

Total words count: **10492 (eFSPC)**

The complete report is submitted for review by the Supervisor and Co-Supervisor.

University Coordinator/
Name & Signature (Checked by)
(From University library)

The complete report of the above thesis has been reviewed by the undersigned. (Check Box)

☐ The similarity index is below accepted norms.

☐ The similarity index is above accepted norms, because of the following reasons:

1.....
2.....
3.....
4.....
5.....

The thesis may be considered for the award of degree. (Relevant documents attached).

Research Scholar **Co-Supervisor** **Supervisor**

INTRODUCTION

Platelet transfusion is an essential component of contemporary oncologic therapeutic treatment and a very successful therapy for hemorrhage in patients with severe thrombocytopenic syndrome. Preventive platelet transfusion has been demonstrated to be highly effective and significant in lowering the risk of bleeding in onco hematological malignancies. Many researches, documents that there is steadily increase of usage of platelet in India with an increasing proportion of single donor apheresis (SDP) products opposed to pooled Random donor platelets (RDP). [1]

Platelet transfusion refractoriness (PTR) means that patient's platelet count is not increasing effectively after platelet transfusion and the clinical bleeding symptoms of patient are not improving [2] and is encountered in upto 30% of the patients that are having hematological disease [3] PTR is frequently seen in oncohematological patients, which exacerbates the supply of platelets, raises the risk of bleeding, and increases demand for platelets. Non-immune reasons account for 60–80% of cases of platelet transfusion refractoriness, however immunological factors can also induce the condition. Immunonological factors plays a role in 10% to 25% of patients include antibodies against four antigen classes HLA class 1 human platelet antigen (HPA), ABO and drug dependent antibodies. [4]

A study showed that leucoreduction lowered HLA alloimmunization from 19% to 7% and alloimmune platelet refractoriness from 14% to 4% for patients undergoing chemotherapy haemat-oncology patients. [4] PTR includes immune and non immune factors. Non immune factors include fever, severe infection, splenomegaly, disseminated intravascular coagulation (DIC), graft versus host disease, vaso-occlusive diseases, and drugs induced thrombocytopenia (Quinidine, penicillin, sulfa drugs, heparin, diuretics, and vancomycin). [5]

Among the immune factors, humoral immunity is currently considered to be the main reason including ABO blood group incompatibility, HLA antigen incompatibility and antibodies produced by platelet specific antigens (HPA) due to prior exposure to transfusion, transplantation, or pregnancy antibodies against these antigens react with transfused donor's platelets and decreases their function and survival [6, 7] Immune destruction is the main reason for PTR. It occurs due to production of antibodies against the specific antigen of platelets in the body which are mainly HLA and HPA antibodies. [8, 9] The majority of clinically relevant HLA antibodies are immunoglobulins IgG(IgG) and are directed against epitopes of class I HLA [10] Immune-mediated platelet refractoriness is primarily caused by alloimmunization with HLA antigen. Platelets that are incompatible can be destroyed and their lifespan decreased by repeated platelet transfusions, which can induce the patient's body to create alloimmunization in response to HPA and HLA class-I antigen. The likelihood of antibody development leading to unsuccessful platelet transfusion increases with the number of transfusions.

Alloimmunization with HLA antigen the primary cause of immune mediated platelet refractoriness. [11] As compared to erythrocyte and granulocyte, platelets have more number of HLA-I Antigen from plasma. [12, 13, 14, 15] Only 2%-8% alloimmunization to HPA antigens is been reported in patients with multiple platelet transfusions. [16, 17] Patients with high anti-A and anti-B antibody titres may have a significant clearance of donor platelets containing relevant ABO antigens. Therefore, transfusion of ABO identical platelets is necessary to prevent this issue.

Also ABO identical are seen to cause more platelet increment as compared to non- identical platelets unit. [9, 18] Because platelets express extremely little of the ABO antigen compared to red blood cells, a patient's ABO antibodies can only cause immunological PTR if they are very high titre. More than 90% of white blood cells are

eliminated by leukocyte reduction, which also has the ability to postpone or stop the commencement of inefficient platelet transfusion brought on by the development of HLA antibodies. Leukofilteration cannot totally stop the formation of antibodies against the HLA-I antigen, which is found on the surface of platelets. Both HPA and HLA class I antibodies can render platelet transfusions ineffective.

Adult patients undergoing therapy for hemato-oncology should use a threshold of $10X10^{9/}l$ for platelet transfusion. The primary clinical symptom of leukemia, a malignant clonal illness of hematopoietic stem cells, is thrombocytopenia. It might happen at the beginning of the treatment or during the period of time when the chemotherapy is suppressing the bone marrow. Life-threatening bleeding can happen in extreme circumstances. Individuals with acute myeloid leukemia who have frequent platelet transfusions: some are more likely to acquire allogenic immunity, which can result in PTR, whereas other individuals never experience immunological PTR.

PTR frequently develops in individuals with acute leukemia, raising the possibility of bleeding. PTR makes the already-limited supply of platelets even scarcer and increases demand for them. Patients with oncohematological malignancies require repeated platelet transfusions; some never acquire immunological PTR, while others are more likely to develop allogenic immunity, which ultimately results in PTR. The patients in these two groups are identical in terms of age and gender. PTR is observed to be more common in patients with AML who have a history of hemophagocytic syndrome, low white blood cell count, extramedullary infiltration, pregnancy, and infection. Those with PTR have a much greater early fatality rate from severe bleeding than those without PTR.

Patients with hematological malignancies who receives multiple platelet transfusions exhibit higher risk of developing PTR. It can be associated with adverse events, including longer hospital stay, severe

hemorrhages and an increased risk of early deaths. [10, 18, 19] Patients with hematological malignancies and Aplastic anemia have a 17–45% incidence of platelet refractoriness despite using leuco reduced blood products.

Leukoreduction involves removal of white cells from blood components, this reduces the risk of developing platelet refractoriness and the need to use HLA matched platelets. [20]

Many mechanisms have been described for drug induced antibody formation, most clinically relevant drug-dependent platelet antibodies are thought to result when a drug interacts with platelet membrane glycoproteins. [21] Drugs commonly implicated are - Abciximab, Carbamazepine, Ceftriaxone, Heparin, Phenytoin, Piperacillin, Quinidine, Quinine, Rifampin, Vancomycin, piperacillin/tazobactam. [22]

We are comparing the effectiveness of platelet concentrate at low and standard doses with single donor platelet apheresis and random donor platelets with the outcome determined by percent platelet recovery and corrected count increment.

Thrombocytopenia in onco hematological illnesses is because of decreased platelet production (due to marrow infiltration by blast cells) and decreased lifespan of platelets. Platelets also have impaired function in such patients due to reduced platelet activation. [23] Thus the platelet transfusion is required to correct thrombocytopenia. Platelet concentrate can be harvested from a single donor (apheresis platelets) or pooled from 4-6 donor's whole blood one unit of apheresis platelet is estimated to increase the platelet count by $30X10^9$/L- $50X10^9$/L, while a single donor unit (before pooling) can increase the platelet count by $5X10^9$/L. [24, 25]

Platelet refractoriness occurs when CCI is less than 7.5 after 1 hour, CCI is less than 4.5 after 24 hours, & PPR is less than 60% after 1 hour, less than 40% after 24 hours of platelet transfusion. [26]

AIM AND OBJECTIVE

- To study the response of standard and low dose of platelets transfusion in onco hematological patients.

REVIEW OF LITERATURE

Thrombocytopenia and hemorrhagic manifestations are brought on by onco-hematological diseases and are a result of bone marrow failure brought on either by the disease process or by the treatment regimen (chemotherapy or radiation).

In such cases platelet transfusion is the main therapy used for the prevention and treatment of hemorrhagic manifestation. [27] Platelet refractoriness is a result of shortened survival of platelets brought about by factors of immunological and or non immunological factors. [28] Since the discovery of platelets in 1881, [29] our knowledge of how they work has grown steadily and more thoroughly. The main purpose of platelets, which are discoid, anucleated cells with a diameter of two to three millimeters, is to regulate hemostasis. Innate immunity and angiogenesis are also important functions of platelets. Despite the fact that around one trillion platelets remain in circulation in adult humans and are replaced every eight to ten days. Megakaryocytes, which are enormous, 30-100 um nucleated cells that are mostly found in the bone marrow, are the source of platelets. Long proplatelet elongations are extended by megakaryocytes during maturation into sinusoidal blood vessles, from which platelets eventually escape.

A delimited plasma membrane, plasma membrane invagination that forms the open canalicular system (OCS), a closed channel network of residual endoplasmic reticulum that forms a dense tubular system (DTS), a cytoskeletal network based on actin and spectrin, a peripheral band of microtubules, and various organelles such as alpha granules, dense granules, peroxisomes, lysosomes, and mitochondria are among the distinguishable structural elements that platelets develop during this process. [24, 25] An adult person has about 1 trillion platelets in circulation, which are tiny anucleated cell fragments designed to stick to injured capillaries, group together, and aid in the production of thrombin.

The GP1b/9/5 complex, which supports platelet adhesion by binding von Willebrand factor, especially in high shear situations, and the alpha2bb3 (GP2b/3a) receptors, which are platelet specific and mediate platelet aggregation by binding fibrinogen and/or von Willebrand factor, are two examples of the activities that contribute to hemostasis by producing platelet plug and then reinforcing plug strength by action of thrombin converting fibrinogen to fibrin strands. [30, 31] Activated platelets release chemokines and a soluble version of CD40 ligand, which trigger an inflammatory response. They also express surface P selection, which promotes contact with leukocytes, and CD40 ligand, which activates several proinflammatory cells.

The production of platelet microparticles, the exposure of negatively charged phospholipids on the surface of platelets, and the release of particular receptors for activated coagulation factors are the causes of platelet coagulant activity. Numerous chemicals that impact vascular tone, wound healing, inflammation, innate immunity, cell proliferation, platelet function, and fibrinolysis are stored in platelets and are actively released upon platelet activation. When platelets are stimulated, new vasoactive and platelet-activating chemicals are created. Because they both initiate and propagate thrombus and are a physical component of the final clot, platelets are essential to hemostasis.

The amount of platelets and agonist-induced aggregation measured in vitro are not very good indicators of bleeding because the complicated environment in which platelets work in vivo is impacted by metabolic abnormalities (such as uremia and sepsis), local vascular malformations, and deficits in coagulation factors.

In the cell based theory of coagulation, platelets provide a rich phospholipid framework for coagulation to occur and after activation platelets release stored coagulation factors. [3] Because haemostasis

depends on platelets, thrombocytopenia causes bleeding that can occasionally be fatal. The bleeding time (BT) assay, initially reported by Duke in 1910, is the only method used for routine clinical evaluation of platelet function in vivo. Harker and Slichter demonstrated that at platelet counts greater than $100X10^9$/l, the BT in individuals with thrombocytopenia—a condition caused by reduced platelet production—remains mostly unchanged. It continues in a linear manner until numbers drop to $10X10^9$/l. The BT is >30 min and unrelated to platelet count for counts of less than $10X10^9$/l. The current practice of transfusing platelets to a threshold of $>50X10^9$/l in surgical patients and those who are bleeding actively is justified by these facts. It is more difficult to understand the biological foundation for using platelets prophylactically.

Hanson and Slichter [32] discovered that platelet survival was significantly decreased at numbers of less than $50X10^9$/l, but only slightly decreased at concentrations between 50 and $100X10^9$/l in in vivo experiments. A two-phase model that took into account the estimated maximum platelet lifespan of 10.5 days, daily platelet loss from senescence (10–15% per day), and the daily requirement of roughly $7.1X10^9$/l platelets for the preservation of "vascular endothelial integrity" were used to explain these data. Hemorrhagic diatheses are caused by quantitative and qualitative abnormalities of the platelets. Uncontrolled platelet thrombus development in pathological situations might result in ischemic tissue necrosis and vasoocclusion. In spite of their comparatively modest size, platelets are crucial for maintaining hemostasis. The first instance in which a transfusion was successful in increasing the platelet count in thrombocytopenic patients.

Two types of platelet concentrate are available for transfusion; one which is the Platelet rich plasma concentrate (PRP-PC) and buffy coat platelet concentrate (BC-PC) are examples of random donor platelets (RDP); the second type is single volunteer thrombocytopheresis donors using an automated cell separator. [32] The main treatment for

thrombocytopenia resulting from several causes is platelet transfusion. While not confirmed, the superiority of SDP versus RDP transfusion is widely believed. These days, there's a growing trend in the use of SDP via apheresis instead than pooled RDP for platelet transfusion therapy.

The use of SDP is preferred over RDP as it represents less donor exposure and, therefore, lowers risk of transmission of virus, alloimmunization, and transfusion associated septic reactions and “better” platelet quality. [33] Platelets need to be transfused more frequently when low doses are used. Therefore, we are evaluating the effectiveness of single donor platelet apheresis with low and standard doses of platelet concentrate. The outcome is determined by corrected count increment and % platelet recovery.

Platelets also have impaired function in such patients due to reduced platelet activation. [23] Thus the platelet transfusion is required to correct thrombocytopenia.

Post-transfusion platelet increase counts must be carefully monitored in order to determine platelet refractoriness.

The corrected count increment (CCI) and percent platelet recovery (PPR) are most frequently used formulas to track the post transfusion increment adjusted for the size of the patient and the dosage administered [34] In both the cases post transfusion platelet count is subtracted from pre transfusion count and then it is divided by the number of platelet transfused. The important difference is that while calculating the CCI, patient’s body surface area is used to normalize the calculation whereas the PPR uses the patient’s volume. Once the refractoriness is been confirmed, immune and non immune causes need to established. A good physical examination helps to rule out the immune causes like active bleeding. DIC, and drug induced thrombocytopenia. Sepsis and fever are involved to cause non immune refractory state. These comorbidities are often present in leukemia

cases, because the chronically thrombocytopenic patients with hematologic disorders are complicated, some immune and non immune factors may present simultaneously [35, 36, 37]

Here, Ethylenediaminetetraacetic acid (EDTA) anticoagulated blood sample is collected for platelet count before transfusion, 1 hour and 24 hrs after transfusion from each patient. [38] The response to transfusion is evaluated by calculating the corrected count increment (CCI) and Percent Platelet Recovery (PPR) one hour and 24 hrs after transfusion as follow

$$\textbf{CCI} = \frac{\text{(platelet increment /ul)X(body surface area in } m^2\text{)X10\^{}11}}{\text{Number of platelet transfused}} = \text{platelets/ul/}m^2$$

$$\textbf{PPR} = \frac{\text{[(platelet concentrate/ul)x(weight in kg x75 ml)]x100}}{\text{Platelet count of products/ul X volume of platelet in ml}} = \text{platelet count \%}$$

1-hr CCI <7.5, 24-hr CCI <4.5, or 1-hr PPR <60%, 24-hr PPR <40% after platelet transfusion is said to be platelet refractoriness. [26]

Platelet transfusion is a vital component of contemporary oncological therapeutic treatment and a very successful therapy for hemorrhage in severely thrombocytopenic patients. One may legitimately claim that the discovery of effective treatments and preventative measures against bleeding in patients with severe myelosuppression and thrombocytopenic patients would be necessary before bone marrow and stem cell transplantation became possible.

According to recent surveys, the number of platelets used in the USA has been rising rapidly; in 1994, there were 1.3 million doses used, and more and more single donor platelets (SDP) products were being used instead of pooled random platelets. [39] By the 1980s when platelet transfusion was available and commonplace, the percentage of adults with acute lymphoblastic leukemia with lethal hemorrhagic

complications had dropped to only 3%. [39] Studies performed in 1970s and 1980s showed that prophylactic transfusion decrease the incidence of significant bleeding episodes in leukemia patients but failed to demonstrate a longer survival in those transfused patients transfused prophylactically as opposed to those transfused only in the presence of bleeding. [40, 41, 42] Most studies of prophylactic use of platelet advocated <20X10^9/l as the appropriate threshold for transfusion. This was usually based on the 1962 publication by Gaydos et.al [43] In contrast; Gmur et al [44] found that the reduction in donor exposure with the use of SDP resulted in reduced alloimmunization. Patients who received single-dose plasma (SDP) were less likely to become refractory than those who received pooled red blood cells (RDP) over longer periods of time and more transfusions. According to the study's conclusion, the use of SDP delays alloimmunization; this could account for the inconsistent results by reducing the average number of donor exposures. In an average-sized adult, a single platelet concentrate containing around 3X10^{11} platelets is projected to boost the platelet count by 30,000–60,000/ul, while an RDP with roughly 7X10^{10} platelets improves the platelet count by 5,000–10,000/ul.

Most institutions adopted policies for “standard” platelet dose to give one platelet concentrate 10kg of body weight and this should increase the platelet count by approximately 40,000/ul. [45] In study patients that developed PTR during induction chemotherapy platelets count was measured daily and transfusion of ABO identical platelet from apheresis products or pooled platelet (0.5-1.0X10^{11} platelet per 10kg) was performed to patients with a platelet count <10X10^9/l to patient with an active bleeding to patients with platelet count <20X10^9/l and fever >38^{oc}. [46, 47, 48] Platelet counts one hour following transfusion termination and the formulas that follow to evaluate transfusion refractoriness are not standard procedures. Consequently, PTR is defined using a clinical definition, which is defined as persistent thrombocytopenia <10X10^9/l despite at least two consecutive daily platelet transfusions. The tests that are available, the frequency of the

patient's HLA type in relation to the pool of HLA matched donors, and the degree of alloimmunization all play a role in matching an appropriate platelet unit for an alloimmunized patient.

Platelet cross matching and HLA matching are frequently uses, the success rate of these strategies is comparable. [49, 50, 51] The quickest and most straightforward method to find a compatible unit is typically the platelet cross match procedure. The patient's serum is combined with a panel of donor platelets in the solid phase red cell adherence assay.

In low resources centres, identification of immune mediated causes of PTR are difficult to diagnose. [27] In well developed centres, the risk of development of PTR because of alloantibodies in patients with multiple transfusions can be determined by microbead flow cytometry. [52] PTR can be diagnosed by lymphocytotoxicity test, enzyme linked immunosorbent assay (ELISA), antigen capture ELISA, platlelet immunoflorescence test (PIFT), or the use of planel reactive antibodies against human leukocyte antigen class I(PRA-HLA). [27] In low setting areas it is not able to ascertained that how patient develops immune mediated alloantibodies to ABO, HLA or HPA antigens on the platlets. [53]

Platelet transfusion refractoriness (PTR) means that patient’s platelet count is not increasing effectively after platelet transfusion and the clinical bleeding symptoms of patient are not improving. [54] and is encountered in upto 30% of the patients that are having hematological disease. [2] PTR includes immune and non immune factors . non immune factors include fever, severe infection, splenomegaly , disseminated intravascular coagulation (DIC), graft versus host disease, vaso-occlusive diseases,and drugs induced thrombocytopenia (Quinidine, penicillin, sulfa drugs, heparin, diuretics, and vancomycin). [5] Both immunological and non-immune variables can contribute to platelet transfusion refractoriness; non-immune

causes account for 60% to 80% of instances. Immunonological factors plays a role in 10% to 25% of patients include antibodies against four antigen classes HLA class 1, human platelet antigen (HPA), ABO and drug dependent antibodies [4]

Among the immune factors, humoral immunity is currently considered to be the main reason including ABO blood group incompatibility, HLA antigen incompatibility and antibodies produced by platelet specific antigens (HPA) due to prior exposure to transfusion, transplantation, or pregnancy antibodies against these antigens react with transfused donor's platelets and decreases their function and survival.[8] Immune destruction is PTR's primary cause. When a patient is not immune, the underlying cause must be addressed .Treatment options in PTR secondary to immune causes include cross matched compatible platelets transfusion, giving HLA matched platelets or identifying the offending alloantibody and transfusing only donor platelets that lack the corresponding antigen. [55, 56]

In low setting areas, it become difficult to determine the presence of HLA or platelet specific alloantibodies. Thus the transfusion of HLA/HPA matched platelets or crossmatched platelet transfusion is not an option for management. Intravenous immunoglobin(IVIg) and Rituximab can be used in immune mediated PTR. [31] It is common in oncohematological patients, which raises the risk of bleeding, intensifies the need for platelets, and worsens the supply of platelets. When anti-HLA and anti-HPA antibodies attach to platelets, they can be seen using an indicator red cell coated in anti-globin G. Immune-mediated platelet refractoriness is primarily caused by alloimmunization with HLA antigen. Platelets and the majority of nucleated cells in the body contain class I HLA molecules, while class II HLA molecules are involved in the presentation of antigens. HLA-A, HLA-B, and HLA-C are the three loci for class I. HLA-A and HLA-B alleles are expressed by platelets, however HLA-C antibodies do not significantly contribute to immune-based refractoriness in clinical settings [14] human platelet

antigens have been identified (HPA). There is less antigenic diversity in the HPA system than in the HLA system, which means that fewer antibodies are involved in immune-based platelet refractoriness. Numerous mechanisms for drug-induced antibody production have been established. Most clinically relevant drug-dependent platelet antibodies are thought to result when a drug interacts with platelet membrane glycoproteins. [21, 22] Drugs commonly implicated are- Abciximab, Carbamazepine, Ceftriaxone, Heparin, Phenytoin, Piperacillin, Quinidine, Quinine, Rifampin, Vancomycin, piperacillin/tazobactam. [57, 58] Patients with high anti-A and anti-B antibody titres may have a significant clearance of donor platelets containing relevant ABO antigens. Therefore, transfusion of ABO identical platelets is necessary to prevent this issue. Also ABO identical are seen to cause more platelet increment as compared to non-identical platelets unit. [9, 18] Patients' ABO antibodies may potentially result in immunological PTR, but only in extreme cases as platelets express very little of the ABO antigen in comparison to red blood cells. In recent studies it has been shown that anti CD36- mediated alloimmune response can produce platelet abnormalities [59, 60, 61] CD36 antigen, is also known as platelet glycoprotein 4(GPIV) and is mainly expressed on platelets and monocytes. This gene can oftenly disappears on cells due to mutations in the expressed gene. There are 2 types of CD36 deficiencies. Among these, in CD36 type I deletion, it disappear from on platelets and monocytes while in type II deletion it becomes undetectable on platelets, thus only type I patients will produce antibodies. [62] The exposure of type I patients to CD36 antigen, such as multiple blood transfusions, pregnancy will result in an alloimmune response to develop CD36 antibodies. [63] Xu.X [64] et al found that CD36 type I deletion and type II deletion are rare in South China population, with an incidence of about 0.5% and 1.3% respectively. [65] The process of HLA and HPA antibodies production is first obtained by antigen presenting cells (APCs) to obtain HLA and HPA and then transfer the antigens information to CD4+ helper T cells, causing T cell activation, and T cells further activate B cells to produce

humoral immunity. [64, 66] In recent years, studies have also shown that CD8+ cytotoxic T cells also play a role in the immune destruction of platelets. [68] More than 90% of white blood cells are eliminated by leukocyte reduction, which also has the ability to postpone or stop the commencement of inefficient platelet transfusion brought on by the development of HLA antibodies. Individuals with multiple platelet transfusions who have hematological malignancies are more likely to acquire PTR. It can be associated with adverse events, including longer hospital stay, severe hemorrhages and an increased risk of early deaths. [18, 19, 69] Patients with hematological malignancies and Aplastic anemia have a 17–45% incidence of platelet refractoriness despite using leucoreduced blood products. Leukoreduction involves removal of white cells from blood components, this reduces the risk of developing platelet refractoriness and the need to use HLA matched platelets [34, 70] It is believed that occurrence of immunological PTR is related to clinical characteristics of acute leukemia and the prognostic stratification of acute leukemia can affect the occurrence of immunological PTR [69] PTR frequently develops in individuals with acute leukemia, raising the possibility of bleeding. PTR makes the already-limited supply of platelets even more scarce and increases demand for them. Patients with oncohematological malignancies require repeated platelet transfusions; some never acquire immunological PTR, while others are more likely to develop allogenic immunity, which ultimately results in PTR. [71, 72] Patients in these two groups are identical in terms of age and gender. Although rituximab, standard dose gamma globulin, and glucocorticoids have been proven to somewhat augment the infusion impact, there are still very few examples of their use. Therefore, more study on alternative approaches to understanding the immunological PTR mechanism is still required.

However, only blood centers with a sizable number of HLA-typed donors and a well-organized inventory can secure a supply of 4/4 matches. Blood banks are forced to recruit known donors when they

are unable to track the HLA type of units in the inventory. This delays the acquisition of units and typically results in a very little supply of platelet units. When exact matches unavailable, one can use the antibody profile determined by the single antigen bead test to select donor units that lack the corresponding cognate antigens (i.e. HLA compatible). [11, 73, 74] In terms of effectiveness, this antibody specificity prediction (ASP) approach is comparable to HLA matching. Furthermore, in comparison to the number of donors available under conventional HLA matching criteria, the ASP technique expands the pool of compatible donors, which facilitates the care of patients with platelet refractoriness. [74]

MATERIAL AND METHODS

Study population included 100 patients who had an adequate platelet response and were unlikely to be refractory to platelet transfusion at the time of enrollment and required multiple platelet transfusion. 25 patients (total 100) received transfusion of standard, low dose of SDP and standard, low dose of RDP in each group respectively.

ABO identical single donor apheresis platelets (SDAPs) was prepared by using, automated cell separator (Trima, Haemonetics)and pooled platelet concentrate was prepared from whole blood donation collected from voluntary donors who qualified the criteria for apheresis platelet donation and whole blood donation as per Directorate General of Health services (DGHS) technical manual. For standard dose, platelet yield of 3-4X10^{11}/unit was harvested. For low dose, apheresis product was split, using sterile connecting device into two products. Pooled platelet concentrate of two units (low dose) and four platelet concentrate units (standard dose) were prepared using sterile connecting device.

A sample of the platelet concentrate (PC) was obtained from the segment tube of the bag in the sterile conditions for the platelet count.

Volume of product (ml)= weight of the product(gm)/ specific gravity

Ethylenediamine tetraacetic acid (EDTA) anticoagulated blood samples were collected for platelet counts after transfusion. The post transfusion counts were assessed after 1hour and 24hrs of transfusion. Corrected count increment (CCI) and percent platelet recovery (PPR) was calculated.

Evaluation of the response to platelet transfusion-

The response to transfusion was calculated by corrected count increment (CCI) and percent platelet recovery (PPR) after 1hour and 24 hrs as follows;

$$\textbf{CCI} = \frac{(\text{Platelet increment /ul}) X (\text{body surface area in } m^2) X 10\text{^}11}{\text{Number of platelet transfused}} = \text{platelets/ul/}m^2$$

$$\textbf{PPR} = \frac{[(\text{platelet increment/ul}) x (\text{weight in kg x75 ml})] x 100}{\text{Platelet count of products/ul X volume of platelet in ml}} = \text{platelet count \%}$$

Platelet increment =Post platelet transfusion count –Pre transfusion count

Estimation of body surface area=$\sqrt{\frac{\text{height(cm)xweight (kg)}}{60}}$

Inclusion criteria-

- Patients without any active bleeding at the time of enrolment.
- Thrombocytopenic hemato-oncology patients and patients on chemotherapy for hemato-oncological malignancies which are non refractory to platelet transfusion.

Exclusion criteria-

Bleeding during study period

Use of drugs affecting platelet number function (eg. Amphotericin B , vancomycin)

Thrombotic thrombocytopenic purpura (TTP)

Hemolytic uremic syndrome (HUS)

Fever or sepsisPatients with splenomegaly and splenectomy

OBSERVATION & RESULTS

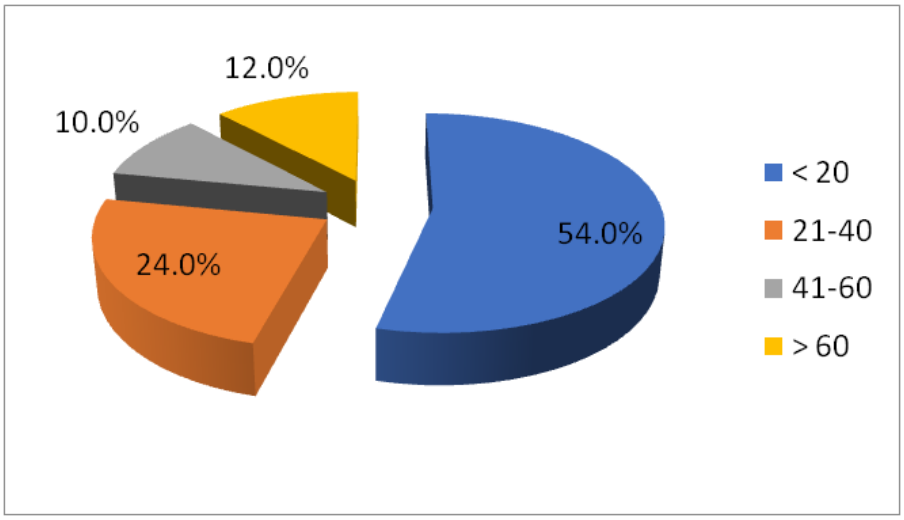

Figure 01: Distribution of Cases Based on Age

In this study population (n=100), 54% (n=54) are of < 20 years of age, 24% (n=24) cases are between 21 to 40 years, 10% (n=10) are between 41-60% and 12% (n=12) cases are above 60 years of age.

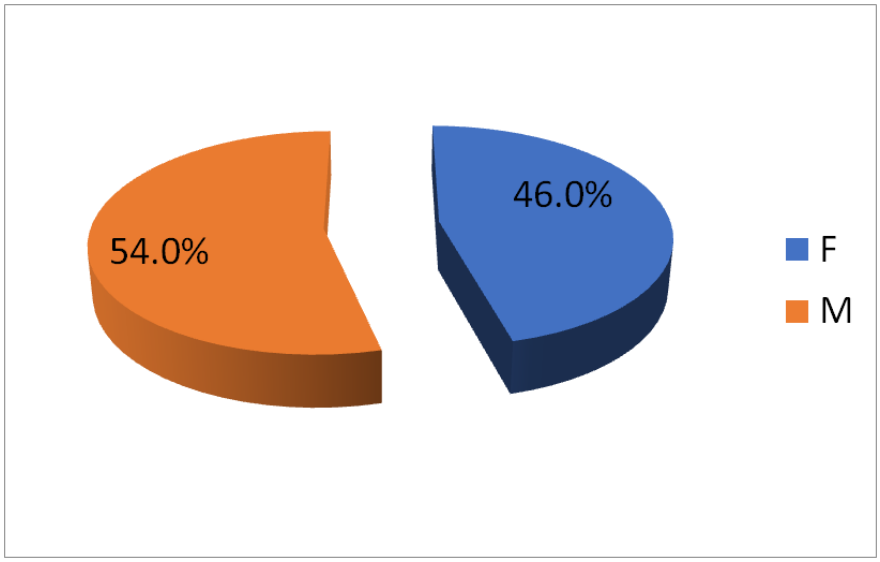

Figure 02: Allocation of Cases Based on Sex

In this study population (n=100), 46% (n=46) cases belongs to female and 54%(n=54) cases are from male group.

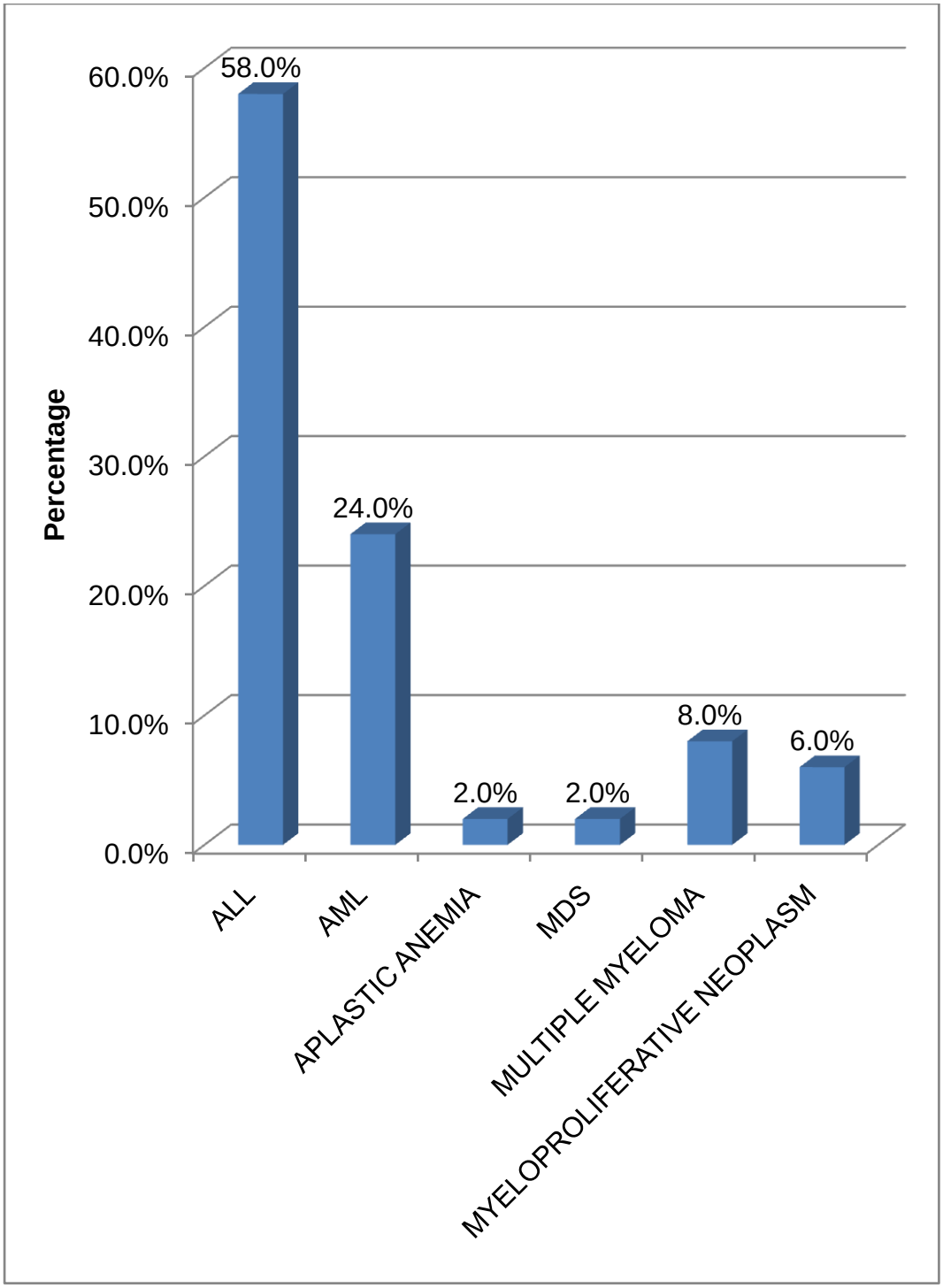

Figure 03: Proportion of Cases Based On Diagnosis

Out of 100 patients, 58% (n=58) are having Acute Lymphocytic Leukemia (ALL), 24% (n=24) have Acute Myeloid Leukemia(AML), 2%(n=2) have Aplastic anaemia, 2%(n=2) have Myelodysplastic syndrome(MDS), 8% (n=8) have Multiple Myeloma, 6% (n=6) cases presented with Myeloproliferative neoplasm .

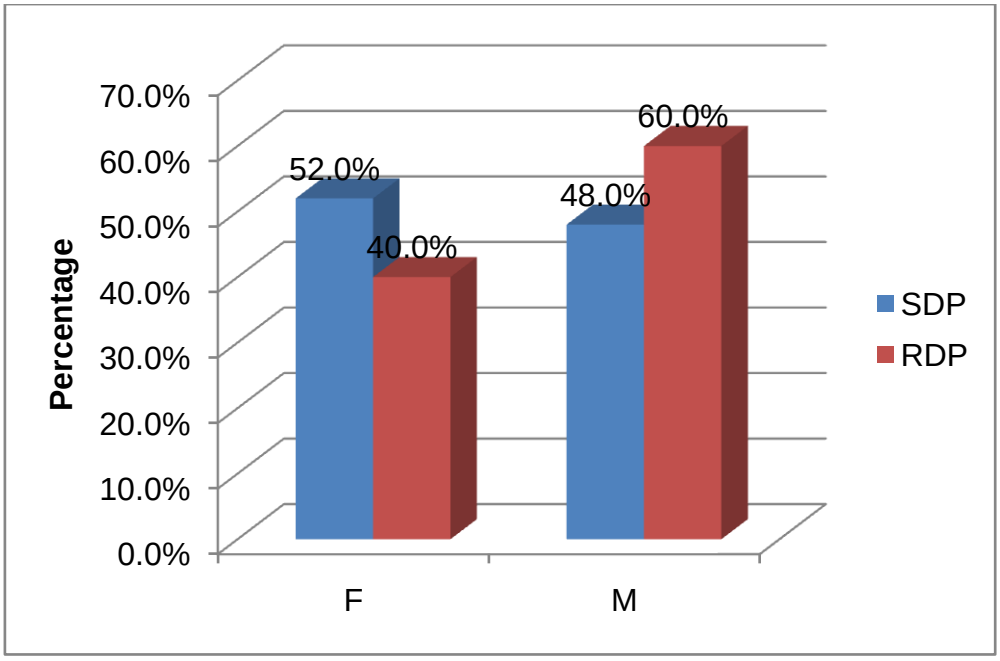

Figure 04: SDP & RDP Transfusion According to Gender

Out of 100 cases, SDP and RDP transfusion is done in both groups with 50 patients in each. In SDP transfusion 52% (n=26) are female and 48% (n=24) are male cases.

While in RDP transfusion 40% (n= 20) are females and 60% (n=30) are males.

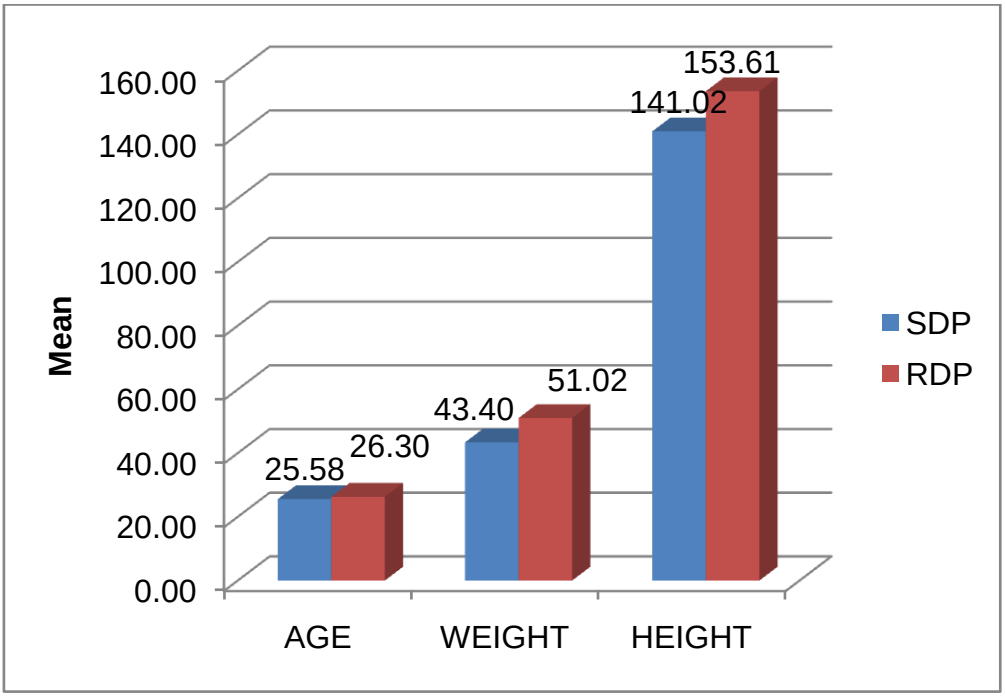

Figure 05: SDP & RDP Transfusion Based on Age, Weight, Height

In SDP transfusion age ranges from 25.58±22.89 years (mean± SD), Weight (kg) 43.40 ±26.72, Height (cm) 141.0± 35.77.

Whereas in RDP transfusion age is in range of 26.30 ±23.14 years,

Weight (kg) 51.02 ±23.70 and Height (cm) 153.61± 24.76.

Table 01: SDP & RDP Transfusion Depending on Diagnosis

		SDP		RDP		Total	Chi-square value	p-value
DIAGNOSIS	ALL	24	48.0%	34	68.0%	58	11.224	0.082
	AML	15	30.0%	9	18.0%	24		
	APLASTIC ANEMIA	0	0.0%	2	4.0%	2		
	MDS	1	2.0%	1	2.0%	2		
	MULTIPLE MYELOMA	4	8.0%	4	8.0%	8		
	MYELOPROLIFERATIVE NEOPLASM	6	12.0%	0	0.0%	6		

In SDP transfusion (n=50), 48% (n=24) have Acute Lymphocytic Leukemia(ALL), 30%(n=15) Acute Myeloid Leukemia(AML), 2%(n=1) Myelodysplastic syndrome, 8%(n=4) Multiple Myeloma, 12%(n=6) Myeloproliferative Neoplasm

While in RDP transfusion (n=50) 68% (n=34) have Acute Lymphocytic Leukemia(ALL), 18% (n=9) Acute Myeloid Leukemia(AML),4%(n=2) Aplastic Anemia, 2%(n=1) Myelodysplastic syndrome, 8%(n=4) Multiple Myeloma.

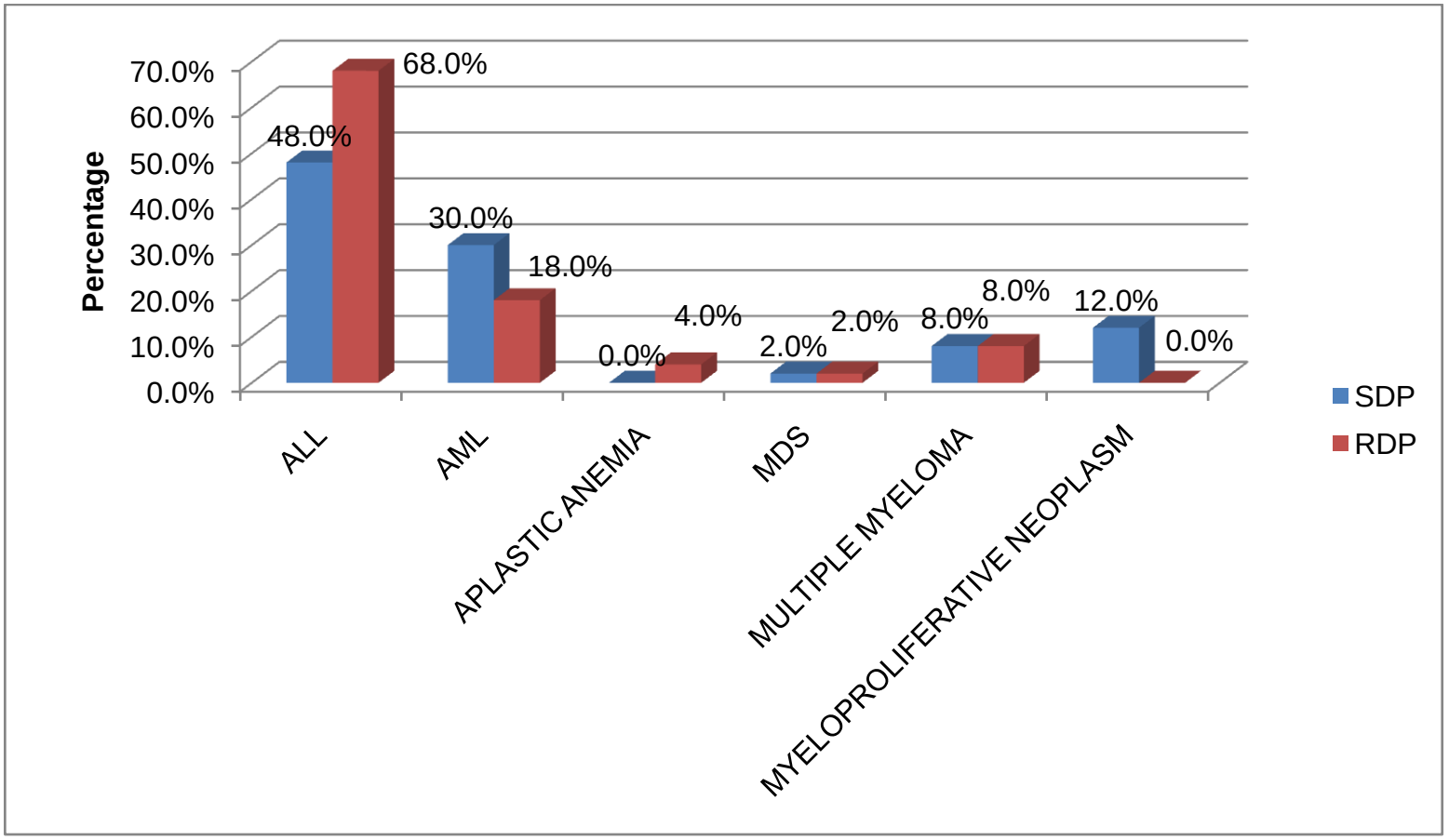

Figure 06: SDP & RDP Transfusion Depending on Diagnosis

Table 02: SDP & RDP Transfusions with Different Doses in Various Onco-Hematological Cases

TYPE		LOW DOSE		STANDARD DOSE		Total	Chi-square value	p-value
		LOW DOSE	LOW DOSE	STANDARD DOSE	STANDARD DOSE			
SDP	ALL	20	80.0%	4	16.0%	24	21.933	0.001
	AML	4	16.0%	11	44.0%	15		
	MDS	0	0.0%	1	4.0%	1		
	MULTIPLE MYELOMA	1	4.0%	3	12.0%	4		
	MYELO-PROLIFERATIVE NEOPLASM	0	0.0%	6	24.0%	6		
RDP	ALL	20	80.0%	14	56.0%	34	6.17	0.187
	AML	4	16.0%	5	20.0%	9		
	APLASTIC ANEMIA	1	4.0%	1	4.0%	2		
	MYELODYSPLASTIC SYNDROME	0	0.0%	1	4.0%	1		
	MULTIPLE MYELOMA	0	0.0%	4	16.0%	4		
		25	100.0%	25	100.0%	50		

In low dose SDP transfusion(n=25), 80%(n=20) have Acute Lymphocytic Leukemia(ALL), 16%(n=04) Acute Myeloid Leukemia(AML), 4%(n=1) Multiple Myeloma. In standard dose SDP transfusion(n=25), 16%(n=4) have Acute Lymphocytic Leukemia(ALL), 44%(n=11) Acute Myeloid Leukemia(AML),4%(n=1) Myelodysplastic syndrome, 12%(n=3) Multiple Myeloma, 24%(n=6) Myeloproliferative Neoplasm.

p value is 0.001 which is significant.

In low dose RDP transfusion(25) 80%(n=20) have Acute Lymphocytic Leukemia(ALL), 16%(n=4) Acute Myeloid Leukemia(AML),4%(n=1) Aplastic Anemia and in standard dose of RDP transfusion(n=25) 56%(n=14) have Acute Lymphocytic Leukemia(ALL), 20%(n=5) have Acute Myeloid Leukemia(AML),4%(n=1) Aplastic Anemia,4%(n=1) Myelodysplastic syndrome, 16%(n=4) Multiple Myeloma

Table 03: Platelet Counts after Transfusion of Different Doses of SDP

SDP	LOW DOSE		STANDARD DOSE		Z	p-value
	Mean	SD	Mean	SD		
PLT DOSEOF PRODUCT $X10^{11}$	2.12	0.15	3.87	0.27	-28.369	0.001
PRE COUNT OF PATIENT$X10^3$/ul	12.06	3.61	11.04	3.52	-0.777	0.437
POST COUNT AFTER 1 HR$X10^3$/ul	42.72	5.29	54.44	16.47	-3.653	0.001
POST COUNT AFTER 24 HR$X10^3$/ul	36.00	6.74	44.72	14.76	-2.885	0.004
PLT INCREMENT 1HR $X10^3$/ul	30.66	5.21	43.40	16.48	-3.778	0.001
PLT INCREMENT 24HR $X10^3$/ul	23.94	7.09	33.68	14.97	-2.894	0.004
CCI 1 HR	12.53	6.81	18.12	8.18	-2.738	0.006
CCI 24 HR	9.15	4.07	14.14	7.16	-2.816	0.005
PPR (%)1 HR	26.72	23.70	50.39	27.12	-3.340	0.001
PPR(%)24 HR	18.76	14.09	39.30	23.35	-3.689	0.000

Platelet count **(X10^{11})** of low dose of SDP unit (mean± SD) is 2.12±0.15.Pre count of patient is 12.06 ± 3.61, Post count after 1 hour is 42.72±5.29, Post count after 24 hrs 36.00± 6.74, Platelet increment after 1 hour is 30.66±5.21 and after 24 hours is 23.94± 7.09. CCI after 1 hour is 12.53±6.81 and 24 hours is 9.15±4.07. PPR after 1 hour is 26.72 ±23.70 and 24 hours is 18.76 ±14.09.

Platelet count **(X10^{11})** of standard dose SDP unit(mean± SD) is 3.87 ±0.27. Pre count in SDP is 11.04 ± 3.52, post count after 1 hour is 54.44±16.47, post count after 24 hrs 44.72± 14.76 Platelet increment after 1 hour is 43.40±16.48 and after 24 hours is 33.68± 14.97. CCI after 1 hour is 18.12±8.18 and 24 hours is 14.14±7.16. PPR after 1 hour is 50.39 ±27.12 and 24 hours is 39.30 ±23.35.

The values which are significant are platelet count of product which is 0.001, post platelet count after 1 hr is 0.001, post platelet count after 24 hr is 0.004. platelet increment after 1 hr is 0.001. Platelet increment after 24 hr is 0.004. CCI after 1 hr is 0.006. CCI after 24 hr is 0.005. PPR after 1 hr is 0.001. PPR after 24 hrs is 0.000.

Table 04: Platelet Counts after Transfusion of Different Doses of RDP

RDP	LOW DOSE		STANDARD DOSE		Z	p-value
	Mean	SD	Mean	SD		
PLT DOSE OF PRODUCT $X10^{11}$	1.64	0.18	3.45	0.29	-26.483	0.001
PRE COUNT OF PATIENT $X10^3$/ul	12.04	3.52	11.36	2.36	-1.178	0.239
POST COUNT AFTER 1 HR $X10^3$/ul	33.28	8.34	54.36	6.55	-6.058	0.001
POST COUNT AFTER 24 HR $X10^3$/ul	27.88	7.21	47.40	7.83	-5.726	0.001
PLT INCREMENT 1HR $X10^3$/ul	21.24	7.25	43.00	7.53	-6.016	0.001
PLT INCREMENT 24HR $X10^3$/ul	15.84	6.13	36.04	8.73	-5.691	0.001
CCI 1 HR	15.63	9.12	21.36	4.57	-2.707	0.007
CCI 24 HR	11.61	7.33	17.86	4.72	-3.192	0.001
PPR (%)1 HR	37.97	31.01	59.71	16.63	-3.192	0.001
PPR(%)24HR	28.23	24.50	49.74	15.30	-3.619	0.000

Platelet count **($X10^{11}$)** of low dose of RDP unit (mean± SD) is 1.64±0.18. Pre count is 12.04 ± 3.52, post count after 1 hour is 33.28±8.34, post count after 24 hrs 27.88± 7.21, platelet increment

after 1 hour is 21.24±7.25 and after 24 hours is 15.84±6.13. CCI after 1 hour is 15.63±9.12and 24 hours is 11.61±7.33. PPR after 1 hour is 37.97 ±31.01 and 24 hours is 28.23 ±24.50.

Platelet count **($X10^3$/ul)** of standard dose RDP unit(mean± SD) is 3.45±0.29. Pre count in RDP is 11.36 ± 2.38, post count after 1 hour is 54.36±6.55, post count after 24 hrs 47.40± 7.83, platelet increment after 1 hour is 43±7.53 and after 24 hours is 36.04± 8.73. CCI after 1 hour is 21.36±4.57 and 24 hours is 17.86±4.72. PPR after 1 hour is 59±16.63 and 24 hours is 49.74±15.30.

The values which are significant are platelet count of product which is 0.001, post platelet count after 1 hr is 0.001, Post platelet count after 24 hr is 0.001. Platelet increment after 1 hr is 0.001. Platelet increment after 24 hr is 0.001. CCI after 1 hr is 0.007. CCI after 24 hr is 0.001. PPR after 1 hr is 0.001. PPR after 24 hr is 0.000.

DISCUSSION

Platelet transfusion is an essential component of contemporary hemato oncologic therapeutic treatment and a very successful therapy for hemorrhage in patients with severe thrombocytopenic syndrome. Preventive platelet transfusion has been demonstrated to be highly effective and significant in lowering the risk of bleeding in oncohematological malignancies. Many researches, documents that there is steadily increase of usage of platelet in India with an increasing proportion of single donor apheresis (SDP) products opposed to pooled Random donor platelets (RDP). [1]

In this study, out of 100 patients, 58% (n = 58) have acute lymphoblastic leukemia (ALL), 24% (n = 24) have acute myeloid leukemia (AML), 2% (n = 2) have aplastic anemia, 2% (n = 2) have myelodysplastic syndrome (MDS), 8% (n = 8) have multiple myeloma, and 6% (n = 6) instances have myeloproliferative neoplasm. Janice P Dutcher et.al [75] studied in 114 patients with acute lymphoblastic leukemia who received multiple platelet transfusions and found that 92% of the patients never become alloimmunized and responded to random donor platelets. There was no difference in age, or sex between groups and prognostic factors predicting alloimmunization. Similar study showed Majority of patients were AML (n = 13, 46.42%) followed by APML (n = 7, 25%), Aplastic anemia (n = 4, 14.2%), multiple myeloma (n = 2, 7.14%) and others like CLL (n = 2), MDS (n = 2), study DLBL (n = 2) and Hodgkin's Lymphoma (n = 2) together as 7.14%. [76] In Unager CA et al [77] study 8 patients were diagnosed with heamto onclogical diseases. Out of which 7 patients were transfused RDP and 1 patient SDP. Similar study was conducted on 105 leukemia patients, out of which 49 patients received transfusion of apheresis platelets and 56 patients received mixed multi person platelet suspension. [78] In Jain N et al [79] study a total of 52 acute leukemia patients received 785 platelet concentrate units (RDP).

Table 05: Comparing the Distribution of Various Malignancies with Other Studies

Study	Janice P Dutcher et.al [75]	Dhiman Y et al [80]	Unager CA et al [77]	Chen LI study et al [86]	**Present study**
AML	NA	13	NA	NA	**24**
ALL	114	NA	NA	NA	**58**
LEUKEMIA	NA	NA	8	105	**NA**
APLASTIC ANEMIA	NA	4	NA	NA	**2**
MYELODYSPLATIC SYNDROME	NA	2	NA	NA	**2**
MULTIPLE MYELOMA	NA	NA	NA	NA	**8**
MYELOPROLIFERATIVE NEOPLASM	NA	NA	NA	NA	**6**

In our study, 25 (total 100) patients received transfusion of standard, low dose of SDP and standard, low dose of RDP in each group respectively.

Platelet count ($X10^{11}$) of standard and low dose of SDP unit is 3.87 ±0.27 and 2.12±0.15 respectively. In Singh RP et al study [81] Platelet dosage of PRP-PC (n=20) was 2.4±0.82X1011, BC-PC(n=20) was 2.2±0.83X1011, apheresis(n=20) was 4.14±1.82X1011.In a study of LI

Chen et al [76] platelet count of apheresis product was $2.5X10^{11}$ Similarly Dhiman Y et al [80] shows platelet count of standard ,low and high dose of SDP was as $3X10^{11}$, $1.5X10^{11}$and $4.5X10^{11}$. Norol F et al [82] reported, platelet count of medium, high and very high dose of SDP was $4.6\pm0.6X10^{11}$, $6.5\pm0.5X10^{11}$ and $8.9\pm0.7X10^{11.}$ Respectively. In comparison to Klumpp TR et al [83] study dosage of platelets for low dose SDP is $3.1X10^{11}$ and high dose is $5X10^{11}$ .Study conducted by Probe et al [84] platelet dose of high dose of SDP was $0.5X10^{11}$/10kg) and double of high dose was $1X10^{11}$/10kg). This study shows the platelet count of Standard and low dose was ($3X10^{11}$and ($1.53x10^{11}$) respectively. [48] In Slichter et al [86] and Plado et al [87] study count of platelets in Low ,standard and high dose was as follow $1.1X10^{11}$, $2.2x10^{11}$and $4.4X10^{11}$.

Pre count of patient before transfusion of standard and low dose of SDP is 11.04 ± 3.52 and 12.06 ± 3.61, which is comparable with the counts of standard, low and very high dose of SDP as 13.071 ± 5.96, 12.416 ± 6.39 and 13.138±7.133. [76] Singh RP et al study [81] conducted study with 7.4±7.1 × 10^3 /µl pre count before SDP transfusion.

After 1 hr, post count with standard dose of SDP is 54.44±16.47 and with low dose is 42.72±5.29 which was similar to the study that showed the post count with SDP 53.4+27.6. [81]

Post counts after 24 hrs, with standard and low dose of SDP transfusion is 44.72± 14.76 and 36.00± 6.74. In Singh RP et al study [81] after 20hrs counts with transfusion of SDP is 46.2+25.1.Similar study had shown - Post count after 20-24 hrs of transfusion with standard, low and high dose of SDP is 36.071 ± 13.64,24.125 ± 12.45 and 35.954 ± 21.03 respectively. [76]

Platelet increment after 1 hr with standard dose of SDP is 43.40±16.48 and with low dose is 30.66±5.21 in comparison to increment with SDP was 43.1+24.2 [81]

Platelet increment after 24 hr with standard and low dose of SDP transfusion is as 33.68± 14.97 and 23.94± 7.09.Similar increment had been shown in a study after 20 hours of SDP transfusion 35.6+22.3 [81] In comparison to plt increment with std ,low and high dose of SDP after 20-24 hrs was 23.000 ± 11.89, 11.708 ± 10.28 and 22.636 ± 18.06 respectively. [81] Francois Norol et al [82] studied plt increment with medium dose ,high and very high dose of SDP and the counts were $33\pm22X10^9$/L , $51\pm29X10^9$/L and $62\pm34X10^9$/L. Klumpp et al [83] reported plt increment with low dose of SDP was $17.01X10^9$/L and with high dose is $37.01X10^9$/L..Similar study was conducted that shows- plt increment with high dose of SDP is $20.8\pm13.5X10^9$/L and with double of high dose was $44.5\pm23.5X10^9$/L . [86]

CCI and PPR after 1 hr with standard dose of SDP is 18.12±8.18and 50.39 ±27.12 and with low dose is 12.53±6.81and is 26.72 ±23.70 which is comparable to a study that shows CCI 16.9+6.3 and PPR 41.1+11.1. [81]

After 24 hrs CCI and PPR with standard dose of SDP is 14.14±7.16 and 39.30 ±23.35 and with low dose is 9.15±4.07 and 18.76 ±14.09. In comparison to a study that found CCI 13.8+6.1 and PPR 33.5+15.2. [81]

Y.Dhiman et al [80] conducted study that shows- CCI with std, low and high dose after 20-24 hrs of SDP transfusion as -12511.50 ± 7384.5, 12279.92 ± 10842.72 and 6979.77 ± 4182.8 and PPR as 35.81 ± 23.23, 35 ± 31.7and 19.9 ± 12.6. Similarly PPR shown with medium dose of SDP is 28±13, high dose 30± 15 and with very high dose 29 ±13. [82] In Probe et al [84] study-CCI with high dose of SDP is 10.6±5.4 and with double of high dose is 12.5±5.

Platelet count ($X10^{11}$) of RDP standard and low dose RDP is 3.45±0.29 and 1.64±0.18. Similar counts were seen in Slichter et al [86] and Plado et al [87] study that showed, in Low dose $1.1X10^{11}$and in Standard dose $2.2x10^{11}$and in High dose $4.4X10^{11}$

Pre count of patient with standard dose of RDP is 11.36 ± 2.38 and with low dose is 12.04 ± 3.52 . In Singh RP et al study [81] pre count of patient before RDP transfusion was $7.4±7.1 \times 10^3$ /µl

After 1 hr post count with standard dose of RDP is 54.36±6.55 and with low is 33.28±8.34. similar study was conducted that showed post count $31.9±14 \times 10^3$ /µl [81]

After 24hrs post counts with RDP transfusion of standard dose is 47.40± 7.83 and with low dose is 27.88± 7.21. Singh RP et al study [81] reported after 20hr counts was 26.1±13.5.

Platelet increment after 1 hr of transfusion with standard dose of RDP is 54.36±6.55 and with low dose is 33.28±8.34. Similar study showed Plt increment was 25±11.9. [81]

After 24 hrs platelet increment with standard dose of RDP is 54.36±6.55 and low dose is 27.88± 7.2and is comparable to the plt increment after 20 hours which was 20.7±11.6. [81]

CCI and PPR after 1 hr with standard dose of RDP is 21.36±4.57 and 59±16.63.With low dose CCI is 15.63±9.12 and PPR is 37.97 ±31.01. Similarly in a study CCI shown was 16.4±1.9 and PPR 36.7±5.5. [81]

After 24 hrs CCI and PPR with standard dose of RDP is 17.86±4.72 and 49.74±15.30.With low dose is 11.61±7.33 and is 28.23 ±24.50.In comparisons to CCI after 20 hrs which was 13.4±1.9 and 30.1±5.4. [81]

Table 05: Comparing the Distribution of Various Malignancies with Other Studies

Study	Jain N Et al [26]	Singh RP Et al [81]	Chen L study et al [76]	Dhiman Y et al [80]	**Present study**
AML	NA	23	NA	13	**24**
ALL	NA	NA	105	NA	**58**
LEUKEMIA	52	NA	NA	NA	**NA**
APLASTIC ANEMIA	NA	25	NA	4	**2**
MYELODYSPLATIC SYNDROME	NA	NA	NA	NA	**2**
MULTIPLE MYELOMA	NA	NA	NA	2	**8**
MYELO-PROLIFERATIVE NEOPLASM	NA	NA	NA	NA	**6**
PLT DOSAGE	RDP 6.45X 10^{10}	RDP-2.2±0.83 × 10^{11}	2.5X10^{11}	std dose-3X10^{11}	**low SDP(2.12±0.15X10^{11})**
		SDP-4.14± 1.82 × 10^{11}		low dose-1.5X10^{11}	**Standard SDP(3.87±0.27X10^{11})**
				high dose-4.5X10^{11}	**low RDP(2units-1.64±0.18X10^{11})**
					Standard RDP(4 units-3.45±0.29X10^{11})

PRE COUNT		7.4±7.1 × 10^3 /µl	NA	std dose-13.071 ± 5.96	**low SDP-12.02±3.61**
				low dose-12.416 ± 6.39	**Std SDP-11.04±3.52**
				high dose-35.954 ± 21.03	**low RDP-12.04±3.52**
					std RDP-11.36±2.36
POST TRANSFUSION (1HR)	NA	(1HR)RDP-31.9±14 × 10^3 /µl	NA	(20-24hr)std dose-36.071 ± 13.64	**low SDP:1 hr-12.53±6.81,RDP-15.63±9.12**
		(1HR)SDP-53.4±27.6		low dose-24.125 ± 12.45	**low SDP:24 hr-9.15±4.07,RDP-11.61±7.33**
				highdose-35.954 ± 21.03	**Std SDP:1 hr-18.12±8.18,RDP-21.36±4.57**
					Std SDP:24 hr -14.14±7.16,RDP-17.86±4.72
POST TRANSFUSION	NA	(20HR) RDP-26.1±13.5			
		(20HR) SDP-46.2±25.1			

INCREMENT(1HR)	NA	(1HR)RDP-25±11.9	NA	std dose-23.000 ± 11.89	**low SDP:1 hr-30.66±5.21,RDP-21.24±7.25**
		(1HR)SDP-43.1±24.2		low dose-11.708 ± 10.28	**low SDP:24 hr-23.94±7.09,RDP-15.84±6.13**
					Std SDP:1 hr-43.40±16.48,RDP-47.40±7.83
					Std SDP:24 hr -33.68±14.97,RDP-36.04±8.73
INCREMENT	9.6	(20HR) RDP-20.7±11.6		high dose-22.636 ± 18.06	
		(20HR) SDP-35.6+22.3			
CCI	NA	(1HR)RDP-16.4±1.9	SDP-12.32±2.09	std dose-12511.50 ± 7384.5	**low SDP:1 hr- 12.53±6.81, RDP-15.63±9.12**
		(1HR)SDP-16.9±6.3	RDP-12.36±2.07	low dose-12279.92 ± 10842.72	**low SDP:24 hr-9.15±4.07, RDP-11.61±7.33**
					Std SDP:1 hr-18.12±8.18, RDP-21.36±4.57
					Std SDP:24 hr -14.14±7.16, RDP-17.86±4.72

CCI	NA	(20HR) RDP-13.4±1.9		high dose-6979.77 ± 4182.8	
		(20HR) SDP-13.8+6.1			
PPR(1HR)	NA	(1HR)RDP-36.7±5.5	SDP-17.34±1.82	std dose-35.81 ± 23.23	**low SDP:1 hr-26.72±23.70,RDP-37.97±31.01**
		(1HR)SDP-41.1±11.1	RDP-17.39±1.83	low dose-35 ± 31.7	**low SDP:24 hr-18.76±14.09,RDP-28.23±24.50**
					Std SDP:1hr-50.39±27.12,RDP-59.71±16.6
					std SDP:24 hr-39.30±23.35,RDP-49.74±15.30
PPR	NA	(20HR) RDP-30.1±5.4		highdose-19.9 ± 12.6	
		(20HR) SDP-33.5±15.2			

Table 07:- Comparison of Platelet Dosages In Different Studies

Study	Francois Norol et al [82]	Klumpp et al [83]	Probe et al [84]	Stop et al [48]	Slichter et al [86]	Plado et al [87]	Tinmouth A et al [88]	**Present study**
No. of patient	69 adults,13 child	46	101	119	1272	1102	111	**100**
Plt dose(plts/unit)	medium(4.6 ±0.6X10^{11})	Low (3.1X 10^{11})	High(0.5X 10^{11}/10kg)	Low(1.53 x10^{11})	Low(1.1 X10^{11})	Low(1.1 X10^{11})	Low (3RDP units)	**low SDP(2.12±0.15 X10^{11})**
	high(6.5±0. 5X10 ^{11})	High (5X10^{11})	Double of high(1X10^{11}/ 10kg)	Standard (3X10^{11})	Standard (2.2x 10^{11})	Standard (2.2X 10^{11})	High (5RDP units)	**Standard SDP(3.87±0.27X10^{1})**
	Very high (8.9±0.7X 10^{11})				High(4.4 X10^{11})	High(4.4 X10^{11})		**low RDP(2units-1.64±0.18X10^{11})**
								Standard RDP (4 units-3.45±0.29 X10^{11})
CCI	NA	NA	10.6±5.4	NA	NA	NA	NA	**low SDP:1 hr-12.53±6.81,RDP-15.63±9.12**
			12.5±5.8					**low SDP:24 hr-9.15±4.07,RDP-11.61±7.33**
								Std SDP:1 hr-18.12±8.18,RDP-21.36±4.57
								Std SDP:24 hr -14.14±7.16,RDP-17.86±4.72

% PPR	28±13	NA	NA	NA	NA	NA	NA	**low SDP:1 hr-26.72±23.70,RDP-37.97±31.01**
	30± 15							**low SDP:24 hr-18.76±14.09,RDP-28.23±24.50**
	29 ±13							**Std SDP:1hr-50.39±27.12,RDP-59.71±16.63**
								std SDP:24 hr-39.30±23.35,RDP-49.74±15.30
Plt incr(X109/L)	33±22X 10^9/L	17.01X1 0^9/L	20.8±13.5X 10^9/L	NA	10.00X 10^9/L	NA	7X 10^9/L	**lowSDP:1hr-30.66±5.21,RDP-21.24±7.25**
	51±29X 10^9/L	37.01X1 0^9/L	44.5±23.5X 10^9/L		19.00X 10^9/L		14X 10^9/L	**low SDP:24hr-23.94±7.09,RDP-15.84±6.13**
	62±34X 10^9/L				38.00X 10^9/L			**std SDP:1HR-43.40±16.48,RDP-59.71±16.63**
								std SDP:24HR-33.68±14.97,RDP-49.74±15.30

SUMMARY AND CONCLUSION

The clinical management of hemato-oncological patients has been greatly enhanced by platelet transfusion, which has resulted in a significant decrease in the death rate from bleeding problems and positive clinical outcomes.

While post-transfusion increments were considerably greater in SDP recipients than in RDP recipients, CCI and PPR were comparable in all patient groups.

Since the post-transfusion response indicators (CCI and PPR) are comparable in all the groups. Low dose may be an option instead of standard dose in stable thrombocytopenic patients. Standard dosage, however, is still a viable option for hemato-oncology patients as the first choice.

Thus from this study it is been concluded that platelets prepared by using any technique are satisfactory. Post-transfusion increases were observed as expected in highly thrombocytopenic people with hemato-oncological illnesses who did not have any confounding variables. While post-transfusion increments were considerably greater in patients receiving larger doses compared to those receiving lower doses. All patient groups' CCI and PPR—which account for the patient's blood volume, increment, and total platelets transfused—were comparable.

SDP may only be advised for a limited number of patients in developing nations because to their high cost and increased technical competence requirements, or in situations where the inventory does not include RDP in sufficient dosages.

BIBLIOGRAPHY

1. Wallace EL, Churchill WH, Surgenor DM, Cho GS, McGurk S. Collection and transfusion of blood and blood components in the United States, 1994. Transfusion. 1998;38:625-36.
2. Christie DJ, Howe RB, Lennon SS, Sauro SC. Treatment of refractoriness to platelet transfusion by protein A column therapy. Transfusion. 1993 Mar;33:234-42.
3. Högman CF, Eriksson L, Wallvik J, Payrat JM. Clinical and laboratory experience with erythrocyte and platelet preparations from a 0.5 CPD Erythro-Sol opti system. Vox sanguinis. 1997 ;73:212-9
4. Cohn CS. Platelet transfusion refractoriness: how do I diagnose and manage?. Hematology 2014, the American Society of Hematology Education Program Book. ;2020:527-32.
5. Ueno H, Klechevsky E, Morita R, Aspord C, Cao T, Matsui T, Et al Dendritic cell subsets in health and disease. Immunological reviews. 2007; 219:118-42.
6. Pavenski K, Freedman J, Semple JW. HLA alloimmunization against platelet transfusions: pathophysiology, significance, prevention and management. Tissue Antigens. 2012; 79:237-45.
7. Rebulla P. A mini-review on platelet refractoriness. Haematologica. 2005;90:247-53
8. Pavenski K, Freedman J, Semple JW. HLA alloimmunization against platelet transfusions: pathophysiology, significance, prevention and management. Tissue Antigens. 2012 ;79:237-45
9. Shehata N, Tinmouth A, Naglie G, Freedman J, Wilson K. ABO-identical versus nonidentical platelet transfusion: a systematic review. Transfusion. 2009;49:2442-53.
10. Yankee RA, Grumet FC, Rogentine GN. Platelet transfusion therapy: The selection of compatible platelet donors for

refractory patients by lymphocyte HL-A typing. New England Journal of Medicine. 1969;281:1208-12.

11. Hod E, Schwartz J. Platelet transfusion refractoriness. British journal of haematology. 2008; 142:348-60
12. Thon JN, Medvetz DA, Karlsson SM, Italiano Jr JE. Road blocks in making platelets for transfusion. Journal of Thrombosis and Haemostasis. 2015;13:S55-62.
13. Gouttefangeas C, Diehl M, Keilholz W, Hörnlein RF, Stevanović S, Rammensee HG. Thrombocyte HLA molecules retain nonrenewable endogenous peptides of megakaryocyte lineage and do not stimulate direct allocytotoxicity in vitro. Blood, The Journal of the American Society of Hematology. 2000; 95:3168-75.
14. Lalezari P, Driscoll AM. Ability of thrombocytes to acquire HLA specificity from plasma.
15. Kao KJ, Scornik JC, Riley WJ, McQueen CF. Association between HLA phenotype and HLA concentration in plasma or platelets. Human immunology. 1988; 21:115-24
16. Duquesnoy RJ, Filip DJ, Rodey GE, Rimm AA, Aster RH. Successful transfusion of platelets “mismatched” for HLA antigens to alloimmunized thrombocytopenic patients. American Journal of Hematology. 1977;2:219-26.
17. Delaflor-Weiss E, Mintz PD. The evaluation and management of platelet refractoriness and alloimmunization. Transfusion medicine reviews. 2000; 14:180-96.
18. Pavenski K, Warkentin TE, Shen H, Liu Y, Heddle NM. Posttransfusion platelet count increments after ABO-compatible versus ABO-incompatible platelet transfusions in noncancer patients: an observational study. Transfusion. 2010;50:1552-60.
19. Meehan KR, Matias CO, Rathore SS, Sandler SG, Kallich J, LaBrecque J, Erder H. Et al Platelet transfusions: utilization and associated costs in a tertiary care hospital. American journal of hematology. 2000;64:251-6.

20. Seftel MD, Growe GH, Petraszko T, Benny WB, Le A, Lee CY. Et al Universal prestorage leukoreduction in Canada decreases platelet alloimmunization and refractoriness. Blood. 2004; 103:333-9.
21. Aster RH, Bougie DW. Drug-induced immune thrombocytopenia. New England Journal of Medicine. 2007; 357:580-7.
22. Bougie DW, Wilker PR, Aster RH. Patients with quinine-induced immune thrombocytopenia have both “drug-dependent” and “drug-specific” antibodies. Blood. 2006 ;108:922-7.
23. Psaila B, Bussel JB, Frelinger AL, Babula B, Linden MD, Li Y. Et al Differences in platelet function in patients with acute myeloid leukemia and myelodysplasia compared to equally thrombocytopenic patients with immune thrombocytopenia. Journal of thrombosis and haemostasis. 2011; 9:2302-10.
24. Fletcher CH, DomBourian MG, Millward PA. Platelet transfusion for patients with cancer. Cancer Control. 2015 Jan;22(1):47-51. Fletcher CH, DomBourian MG, Millward PA. Platelet transfusion for patients with cancer. Cancer Control. 2015; 22:47-51.
25. Trial to Reduce Alloimmunization to Platelets Study Group. Leukocyte reduction and ultraviolet B irradiation of platelets to prevent alloimmunization and refractoriness to platelet transfusions. New England Journal of Medicine. 1997;337:1861-70.
26. Kerkhoffs JL, Eikenboom JC, Van De Watering LM, Van Wordragen-Vlaswinkel RJ, Wijermans PW, Brand A. The clinical impact of platelet refractoriness: correlation with bleeding and survival. Transfusion. 2008;48:1959-65
27. Ferreira AA, Zulli R, Soares S, Castro VD, Moraes-Souza H. Identification of platelet refractoriness in oncohematologic patients. Clinics. 2011; 66: 35-40.
28. Slichter SJ, Davis K, Enright H, Braine H, Gernsheimer T, Kao KJ, Et al Factors affecting posttransfusion platelet increments,

platelet refractoriness, and platelet transfusion intervals in thrombocytopenic patients. Blood. 2005; 105:4106-14.

29. Lichtman MA,Liesveld JL.acute myelogenous leukaemia chapter 89 in kaushansky K, Lichtman MA, Beutler E, Kipps TJ, Seligsohn U, Prchal JT, Wiliiam Hematology , McGraw Hill Medical
30. Ferreira AA, Zulli R, Soares S, Castro VD, Moraes-Souza H. Identification of platelet refractoriness in oncohematologic patients. Clinics. 2011;66:35-40.
31. Cid J, Magnano L, Acosta M, Alba C, Esteve J, Lozano M. Et al plasma exchange and intravenous immunoglobulins as a new treatment strategy for severe HLA alloimmune platelet refractoriness. Platelets. 2015; 26:190-4.
32. Slichter SJ. Platelet transfusion therapy. Hematology/oncology clinics of North America. 1990; 4:291-311.
33. Wallace EL, Churchill WH, Surgenor DM, An J, Cho G, McGurk S, Et al. Collection and transfusion of blood and blood components in the United States, 1992. Transfusion. 1995 ;35:802-12
34. Bishop JF, Matthews JP, Yuen K, McGrath K, Wolf MM, Szer J. The definition of refractoriness to platelet transfusions. Transfusion Medicine. 1992; 2:35-41.
35. Sullivan MT, Cotten R, Read EJ, Wallace EL. Blood collection and transfusion in the United States in 2001. Transfusion. 2007 Mar;47:385-94.
36. Vassallo Jr RR. New paradigms in the management of alloimmune refractoriness to platelet transfusions. Current opinion in hematology. 2007; 14:655-63.
37. O'connell B, Lee EJ, Schiffer CA. The value of 10-minute posttransfusion platelet counts. Transfusion. 1988; 28:66-7.
38. Legler TJ, Fischer I, Dittmann J, Simson G, Lynen R, Humpe A, Et al Frequency and causes of refractoriness in multiply transfused patients. Annals of hematology. 1997; 74:185-9.

39. Benjamin RJ, Anderson KC. What is the proper threshold for platelet transfusion in patients with chemotherapy-induced thrombocytopenia? Critical reviews in oncology/hematology. 2002; 42:163-71.
40. Higby DJ, Cohen E, Holland JF, Sinks L. The prophylactic treatment of thrombocytopenic leukemic patients with platelets: a double blind study. Transfusion. 1974; 14:440-6.
41. Roy AJ, Jaffe N, Djerassi I. Prophylactic platelet transfusions in children with acute leukemia: a dose response study. Transfusion. 1973; 13:283-90.
42. Murphy S, Litwin S, Herring LM, Koch P, Remischovsky J, Donaldson MH. Et al Indications for platelet transfusion in children with acute leukemia. American journal of hematology. 1982; 12:347-56.
43. Gaydos LA, Freireich EJ, Mantel N. The quantitative relation between platelet count and hemorrhage in patients with acute leukemia. New England Journal of Medicine. 1962; 266:905-9.
44. Gmur J, von Felten A, osterwalder B, et.al. delayed alloimmunization using random single platelet transfusion: identification of a large group of patients who do not become alloimmunized. Blood 1981;58:1007-11
45. Schiffer CA, Anderson KC, Bennett CL, Bernstein S, Elting LS, Goldsmith M. Et al Platelet transfusion for patients with cancer: clinical practice guidelines of the American Society of Clinical Oncology. Journal of clinical oncology. 2001 Mar 1;19(5):1519-38.
46. Haute Autorite de santé, transfusion De Plaquettes; Produites indications; recommendations De Bonne Pratique Clinique, (2015).
47. Ness PM, Campbell-Lee SA. Single donor versus pooled random donor platelet concentrates. Current opinion in hematology. 2001; 8:392-6.

48. Goodnough LT, Kuter D, McCullough J, Brecher ME. Apheresis platelets: emerging issues related to donor platelet count, apheresis platelet yield, and platelet transfusion dose. Journal of clinical apheresis. 1998; 13:114-9.
49. Moroff G, Garratty G, Heal JM, MacPherson BR, Stroncek D, Huang ST. Et al Selection of platelets for refractory patients by HLA matching and prospective crossmatching. Transfusion. 1992; 327:633-40.
50. Rioux-Massé B, Cohn C, Lindgren B, Pulkrabek S, McCullough J. Utilization of cross-matched or HLA-matched platelets for patients refractory to platelet transfusion. Transfusion. 2014; 54:3080-7.
51. Seike K, Fujii N, Asano N, Ohkuma S, Hirata Y, Fujii K. Et al Efficacy of HLA virtual cross-matched platelet transfusions for platelet transfusion refractoriness in hematopoietic stem cell transplantation. Transfusion. 2020; 60:473-8.
52. Beligaswatte A, Tsiopelas E, Humphreys I, Bennett G, Robinson K, Davis K, Bardy P. The mean fluorescence intensities of anti-HLA antibodies detected using micro-bead flow cytometry predict the risk of platelet transfusion refractoriness. British journal of haematology. 2013;162:409-12.
53. Tinmouth AT, Semple E, Shehata N, Branch DR. Platelet immunopathology and therapy: a Canadian Blood Services research and development symposium. Transfusion Medicine Reviews. 2006;4:294-314.
54. Forest SK, Hod EA. Management of the platelet refractory patient. Hematology/Oncology Clinics. 2016; 30:665-77.
55. Adewoyin AS, Oyewale OA. Complications of allogeneic blood transfusion: Current approach to diagnosis and management. International Blood Research & Reviews. 2015;3:135-51.
56. Hod E, Schwartz J. Platelet transfusion refractoriness. British journal of haematology. 2008; 142:348-60.

57. Reese JA, Li X, Hauben M, Aster RH, Bougie DW, Curtis BR. Et al identifying drugs that cause acute thrombocytopenia: an analysis using 3 distinct methods. Blood, The Journal of the American Society of Hematology. 2010;116:2127-33.
58. Bougie D, McFarland J, Curtis B, Aster R. Drug-induced immune thrombocytopenia: results of the testing for drug-dependent platelet-reactive antibodies by the BloodCenter of Wisconsin, 1995-2018.
59. Holbro A, Infanti L, Sigle J, Buser A. Platelet transfusion: basic aspects. Swiss Med Wkly. 2013 ;143
60. Hayashi T, Hirayama F. Advances in alloimmune thrombocytopenia: perspectives on current concepts of human platelet antigens, antibody detection strategies, and genotyping. Blood Transfusion. 2015;13:380.
61. Moncharmont P. Platelet component transfusion and alloimmunization: where do we stand?. Transfusion Clinique et Biologique. 2018; 25:172-8.
62. Yamamoto N, Akamatsu N, Sakuraba H, Yamazaki H, Tanoue K. Platelet glycoprotein IV (CD36) deficiency is associated with the absence (type I) or the presence (type II) of glycoprotein IV on monocytes.
63. Schmidt AE, Sahai T, Refaai MA, Sullivan M, Curtis BR. Severe platelet transfusion refractoriness in association with antibodies against CD36. Laboratory Medicine. 2020; 51:540-4.
64. Xu X, Ye X, Xia W, Liu J, Ding H, Deng J. Et al Studies on CD36 deficiency in South China: two cases demonstrating the clinical impact of anti-CD36 antibodies. Thrombosis and haemostasis. 2013; 110:1199-206.
65. Xia W, Ye X, Xu X, Ding H, Liu J, Deng J. Et al Two cases of platelet transfusion refractoriness and one case of possible FNAIT caused by antibodies against CD36 in China. Transfusion Medicine. 2014;24

66. Freireich EJ, Schmidt PJ, Schneiderman MA, Frei III E. A comparative study of the effect of transfusion of fresh and preserved whole blood on bleeding in patients with acute leukemia. New England Journal of Medicine. 1959 Jan 1;260:6-11.
67. Manis JP, Silberstein LE. Platelet refractoriness: it's not the B-all and end-all. Blood. 2016 ;127:1740-1
68. Arthur CM, Patel SR, Sullivan HC, Winkler AM, Tormey CA, Hendrickson JE. Et al CD8+ T cells mediate antibody-independent platelet clearance in mice. Blood. 2016;127:1823
69. Zhou Z, Gao Y, Li X, Ren J, Liu Y, Li J. The clinical characteristics of patients with acute leukemia or stem cell transplantation exhibiting immune based platelet refractoriness. Transfusion and Apheresis Science. 2020;59:10272
70. Bassuni WY, Blajchman MA, Al-Moshary MA. Why implement universal leukoreduction?. Hematology/oncology and stem cell therapy. 2008; 1:106-23.
71. Anderson NA, Gray S, Copplestone JA, Chan DC, Hamon M, Prentice AG. Et al A prospective randomized study of three types of platelet concentrates in patients with haematological malignancy: corrected platelet count increments and frequency of nonhaemolytic febrile transfusion reactions. Transfusion Medicine. 1997; 7:33-9.
72. Gurkan E, Patah PA, Saliba RM, Ramos CA, Anderson BS, Champlin R. Et al Efficacy of prophylactic transfusions using single donor apheresis platelets versus pooled platelet concentrates in AML/MDS patients receiving allogeneic hematopoietic stem cell transplantation. Bone marrow transplantation. 2007; 40:461-4.
73. Vassallo Jr RR. New paradigms in the management of alloimmune refractoriness to platelet transfusions. Current opinion in hematology. 2007;14:655-63.

74. Petz LD, Garratty G, Calhoun L, Clark BD, Terasaki PI, Gresens C. Et al Selecting donors of platelets for refractory patientson the basis of HLA antibody specificity. Transfusion. 2000; 40:1446-56.

75. Dutcher JP, Schiffer CA, Aisner J, Wiernik PH. Long-term follow-up of patients with leukemia receiving platelet transfusions: Identification of a large group of patients who do not become alloimmunized. Blood. 1981; 58:1007-11.

76. Chen L, Zhou H, Guo B, Guan Z. Clinical efficacy of platelet transfusion therapy in patients with leukemia and analysis of risk factors for ineffective transfusion. Oncology Letters. 2020; 19:2554-61.

77. Unagar CA, Patel SG, Patel KA, Pandya AN, Jarag MA, Patel JN. Et al Transfusion effect of random donor platelet and single donor platelet in thrombocytopenic patients at tertiary care hospital of South Gujarat. Int J Res Med Sci. 2017; 5:3033-7.

78. Ren J, Li J, Liu Y, Zhou Z. Research progress on the immunological platelet transfusion refractoriness in patients with acute leukemia: a narrative review. Annals of Blood. 2021 ; 6.

79. Jain N, De D, Aujla R. Effectiveness of Random Donor Platelet (RDP) Transfusion Therapy in Acute Leukaemia Patients: A Retrospective Analysis. Ann Hematol Onco. 2023; 10: 1428.

80. Dhiman Y, Hans R, Sharma RR, Malhotra P, Marwaha N. Comparison of efficacy of low and high dose prophylactic platelet transfusion therapy in thrombocytopenic haemato-oncology patients. Transfusion and Apheresis Science. 2020; 59:102610.

81. Singh RP, Marwaha N, Malhotra P, Dash S. Therapeutic efficacy of different types of platelet concentrates in thrombocytopenic patients. Indian Journal of Hematology and Blood Transfusion. 2008; 24:16-22.

82. Norol F, Bierling P, Roudot-Thoraval F, Le Coeur FF, Rieux C, Lavaux A. Et al Platelet transfusion: a dose-response study. Blood, the Journal of the American Society of Hematology. 1998; 92:1448-53.
83. Klumpp TR, Herman JH, Gaughan JP, Russo RR, Christman RA, Goldberg SL, Ackerman SJ, Bleecker GC, Mangan KF. Clinical consequences of alterations in platelet transfusion dose: a prospective, randomized, double-blind trial. Transfusion. 1999; 39:674-81.
84. Sensebé L, Giraudeau B, Bardiaux L, Deconinck E, Schmidt A, Bidet ML. Et al The efficiency of transfusing high doses of platelets in hematologic patients with thrombocytopenia: results of a prospective, randomized, open, blinded end point (PROBE) study. Blood. 2005; 105:862-4.
85. Kerkhoffs JL, Eikenboom JC, Van De Watering LM, Van Wordragen-Vlaswinkel RJ, Wijermans PW, Brand A. The clinical impact of platelet refractoriness: correlation with bleeding and survival. Transfusion. 2008; 48:1959-65.
86. Slichter SJ, Kaufman RM, Assmann SF, McCullough J, Triulzi DJ, Strauss RG. Et al Dose of prophylactic platelet transfusions and prevention of hemorrhage. New England Journal of Medicine. 2010; 362:600-13.
87. Kaufman RM, Assmann SF, Triulzi DJ, Strauss RG, Ness P, Granger S. Et al. Transfusion-related adverse events in the P latelet Dose study. Transfusion. 2015; 55:144-53.
88. Tinmouth A, Tannock IF, Crump M, Tomlinson G, Brandwein J, Minden M. Et al Low-dose prophylactic platelet transfusions in recipients of an autologous peripheral blood progenitor cell transplant and patients with acute leukemia: a randomized controlled trial with a sequential Bayesian design. Transfusion. 2004; 44:1711-9.

SR. NO.	NAME	MRD NO.	AGE	SEX	WEIGHT	HEIGHT	BSA	DIAGNOSIS	TREATMENT	PRE COUNT	POST COUNT 1 HR	POST COUNT 24 HR	PLT INCREMENT 1HR	PLT INCREMENT 24HR	CCI 1 HR	CCI 24 HR	PPR 1 HR	PPR24 HR	PLT COUNT OF PRODUCT/ UL	VOL OF PLT IN ML	No. of PLT transfused	SDP UNIT NO.	SDP DOSE	RDP UNIT NO.	RDP DOSE
1	S	1481884	14	F	30	121	1.00	AML	Chemotherapy	14	45	42	31	28	13.30	12.02	29.8	26.9	1800	130	1	2560	LOW	—	—
2	KG	820404	15	F	50	157	1.48	AML	Chemotherapy	8	38	24	30	16	20.65	11.01	52.4	28.0	850	130	1	2212	LOW	—	—
3	PA	1582896	4	M	13	196	0.84	ALL	Chemotherapy	12	40	32	28	20	11.78	8.41	13.7	9.8	715	125	1	1699	LOW	—	—
4	MK	1570050	29	F	29	157	1.12	ALL	Chemotherapy	10	40	32	30	22	14.92	10.94	28.8	21.2	987	130	1	657	LOW	—	—
5	AS	1564906	57	M	78	167	1.90	MULTIPLE MYELOMA	Chemotherapy	14	48	31	34	17	31.36	15.68	96.4	48.2	889	125	1	2456	LOW	—	—
6	K	1569678	2	M	7	80	0.39	ALL	Chemotherapy	14	46	40	32	26	5.34	4.34	7.1	5.8	988	135	1	244	LOW	—	—
7	K	1569678	2	M	10	85	0.49	ALL	Chemotherapy	10	47	40	37	30	8.64	7.01	13.3	10.8	899	130	1	145	LOW	—	—
8	GS	1575462	14	M	69	152	1.71	ALL	Chemotherapy	12	46	38	34	26	28.45	21.75	86.3	66.0	987	120	1	130	LOW	—	—
9	P	1331711	6	F	20	115	0.80	ALL	Chemotherapy	10	35	28	25	18	9.25	6.66	17.4	12.5	873	135	1	149	LOW	—	—
10	K	1569678	2	M	10	85	0.49	ALL	Chemotherapy	7.4	40	38	32.6	30.6	9.00	8.45	13.9	13.0	965	110	1	155	LOW	—	—
11	JV	1553325	25	M	58	172	1.66	ALL	Chemotherapy	12	35	26	23	14	17.85	10.86	46.6	28.4	1021	130	1	170	LOW	—	—
12	JV	153325	25	M	58	172	1.66	ALL	Chemotherapy	20	36	31	16	11	12.53	8.62	32.8	22.5	983	125	1	185	LOW	—	—
13	S	1481884	14	F	47	158	1.44	AML	Chemotherapy	14	45	30	31	16	19.57	10.10	48.0	24.8	899	130	1	192	LOW	—	—
14	V	1540531	1	M	11	52	0.40	ALL	Chemotherapy	6	42	38	36	32	6.69	5.95	13.8	12.3	973	130	1	195	LOW	—	—
15	VT	1540531	1	M	11	85	0.51	ALL	Chemotherapy	12	50	48	38	36	9.39	8.90	15.2	14.4	879	125	1	198	LOW	—	—
16	SD	1491673	3	M	11	90	0.52	ALL	Chemotherapy	14	47	30	33	16	7.83	3.80	12.3	6.0	843	130	1	220	LOW	—	—
17	P	1582896	4	F	15	198	0.91	ALL	Chemotherapy	8	32	31	24	23	11.80	11.30	14.6	14.0	876	110	1	1699	LOW	—	—
18	P	1582896	4	F	13	96	0.59	ALL	Chemotherapy	14	36	28	22	14	5.96	3.79	9.9	6.3	971	125	1	1224	LOW	—	—
19	V	1540531	1	M	11	85	0.51	ALL	Chemotherapy	14	50	46	36	32	7.84	6.97	12.7	11.3	875	130	1	1370	LOW	—	—
20	JV	1553325	1	M	7	75	0.38	ALL	Chemotherapy	18	48	42	30	24	5.62	4.49	7.7	6.2	964	120	1	1401	LOW	—	—
21	VS	1593306	9	M	26	130	0.97	ALL	Chemotherapy	10	45	42	35	32	18.43	16.85	37.1	33.9	854	115	1	1530	LOW	—	—
22	MR	1598180	8	M	23	126	0.90	ALL	Chemotherapy	10	42	41	32	31	13.47	13.05	25.9	25.1	987	130	1	1367	LOW	—	—
23	PA	1582896	4	F	13	196	0.84	ALL	Chemotherapy	18	50	45	32	27	12.97	10.94	15.0	12.7	1098	120	1	1356	LOW	—	—
24	SS	1463278	4	M	13	95	0.59	ALL	Chemotherapy	14	45	42	31	28	8.54	7.72	14.2	12.8	953	125	1	1369	LOW	—	—
25	MK	1403827	2	M	12	86	0.54	AML	Chemotherapy	6	40	35	34	29	7.96	6.79	13.4	11.4	897	130	1	1670	LOW	—	—
26	HS	1433542	22	F	84	164	1.96	AML	Chemotherapy	12	26	22	14	10	6.60	4.71	21.3	15.2	1121	250	1	118	HIGH	—	—
27	CK	1483190	53	F	50	152	1.45	MYELOPROLIFERTIVE	Chemotherapy	16	76	56	60	40	24.42	16.28	63.0	42.0	1325	210	1	120	HIGH	—	—
28	CK	1483190	53	F	50	152	1.45	MYELOPROLIFERTIVE	Chemotherapy	14	48	42	34	28	12.83	10.57	33.1	27.3	1120	220	1	124	HIGH	—	—
29	CK	1493190	53	F	50	152	1.45	MYELOPROLIFERTIVE	Chemotherapy	10	47	36	37	26	13.58	9.54	35.0	24.6	984	220	1	126	HIGH	—	—
30	HK	1433542	22	F	82	165	1.94	AML	Chemotherapy	10	66	56	56	46	28.61	23.50	90.8	74.5	898	230	1	206	HIGH	—	—
31	V	1540531	32	M	68	168	1.78	ALL	Chemotherapy	6	58	45	52	39	22.06	16.54	63.1	47.4	1001	240	1	2314	HIGH	—	—
32	HK	1631440	31	F	58	160	1.61	AML	Chemotherapy	13	60	42	47	29	20.18	12.45	54.7	33.7	1343	220	1	2390	HIGH	—	—
33	AP	1610837	7	M	20	120	0.82	AML	Chemotherapy	4	58	50	54	46	11.66	9.94	21.4	18.3	1001	210	1	2294	HIGH	—	—
34	AP	1610837	7	M	20	120	0.82	AML	Chemotherapy	6	54	49	48	43	11.26	10.09	20.7	18.5	954	200	1	2173	HIGH	—	—
35	KG	820404	54	F	50	157	1.48	MULTIPLE MYELOMA	Chemotherapy	6	36	22	30	16	11.08	5.91	28.1	15.0	987	250	1	2209	HIGH	—	—
36	JK	1016336	85	M	78	170	1.92	AML	Chemotherapy	13	74	60	61	47	32.25	24.85	98.3	75.7	1016	220	1	1931	HIGH	—	—

SR. NO.	NAME	MRD NO.	AGE	SEX	WEIGHT	HEIGHT	BSA	DIAGNOSIS	TREATMENT	PRE COUNT	POST COUNT 1 HR	POST COUNT 24 HR	PLT INCREMENT 1HR	PLT INCREMENT 24HR	CCI 1 HR	CCI 24 HR	PPR 1 HR	PPR24 HR	PLT COUNT OF PRODUCT/ UL	VOL OF PLT IN ML	No. of PLT transfused	SDP UNIT NO.	SDP DOSE	RDP UNIT NO.	RDP DOSE
37	H	1631440	31	F	58	160	1.61	AML	Chemotherapy	15	22	16	7	1	2.68	0.38	7.3	1.0	1122	240	1	2419	HIGH	—	—
38	HS	1144127	74	M	87	170	2.03	MDS	Chemotherapy	12	11	12	-1	0	-0.50	0.00	-1.6	0.0	1321	240	1	631	HIGH	—	—
39	KB	941380	31	M	85	170	2.00	ALL	Chemotherapy	14	66	58	52	44	30.07	25.44	95.7	81.0	1281	210	1	1247	HIGH	—	—
40	HK	1433542	22	F	82	165	1.94	AML	Chemotherapy	10	40	28	30	18	16.52	9.91	52.4	31.4	1189	220	1	2064	HIGH	—	—
41	PK	1493133	39	F	65	160	1.70	AML	Chemotherapy	10	65	59	55	49	23.91	21.30	68.6	61.1	957	230	1	1218	HIGH	—	—
42	CK	1483190	53	F	50	152	1.45	MYELOPROLIFERATIVE NEOPLASM	Chemotherapy	14	58	48	44	34	14.80	11.44	38.2	29.5	1202	240	1	124	HIGH	—	—
43	HK	1433542	22	F	84	154	1.90	AML	Chemotherapy	13	68	61	55	48	25.27	22.06	84.0	73.3	978	250	1	2129	HIGH	—	—
44	HK	1433542	22	F	84	154	1.90	AML	Chemotherapy	16	72	62	56	46	25.93	21.30	86.2	70.8	900	230	1	1160	HIGH	—	—
45	CK	1483190	53	F	50	152	1.45	MYELOPROLIFERATIVE NEOPLASM	Chemotherapy	16	59	44	43	28	17.21	11.21	44.4	28.9	1016	220	1	120	HIGH	—	—
46	CK	1483190	53	F	50	152	1.45	MYELOPROLIFERATIVE NEOPLASM	Chemotherapy	10	50	36	40	26	15.79	10.27	40.8	26.5	1234	230	1	128	HIGH	—	—
47	GB	1553468	38	M	68	167	1.78	ALL	Chemotherapy	8	60	52	52	44	26.65	22.55	76.5	64.8	1201	210	1	1888	HIGH	—	—
48	KD	1544786	42	F	48	160	1.46	MULTIPLE MYELOMA	Chemotherapy	10	68	60	58	50	21.67	18.68	53.4	46.0	999	230	1	1378	HIGH	—	—
49	RC	433115	62	F	52	162	1.53	MULTIPLE MYELOMA	Chemotherapy	6	56	50	50	44	19.92	17.53	50.8	44.7	1287	240	1	1541	HIGH	—	—
50	RC	433115	67	F	52	162	1.53	ALL	Chemotherapy	12	63	52	51	40	18.36	14.40	46.8	36.7	1045	250	1	918	HIGH	—	—
51	HK	1433542	22	F	84	164	1.96	AML	Chemotherapy	12	35	30	23	18	35.15	27.51	113.2	88.6	800	160	2			116087, 116089	LOW
52	SK	1491085	20	M	60	183	1.75	ALL	Chemotherapy	10	35	30	25	20	28.54	22.83	73.5	58.8	900	180	2			118885, 118883	LOW
53	SK	1491085	20	M	60	183	1.75	ALL	Chemotherapy	12	36	31	24	19	26.20	20.74	67.5	53.4	1128	160	2			118717, 118802	LOW
54	JK	1247624	15	F	28	121	0.97	ALL	Chemotherapy	14	38	32	24	18	13.62	10.21	29.5	22.1	845	180	2			123454, 123456	LOW
55	SK	935269	8	F	16	117	0.72	ALL	Chemotherapy	16	40	34	24	18	11.84	8.88	19.7	14.8	1125	170	2			123383, 123451	LOW
56	HS	1418406	4	M	14.6	99	0.63	ALL	Chemotherapy	18	40	36	22	18	9.68	7.92	16.7	13.7	1142	180	2			123767, 123766	LOW
57	KB	941380	11	M	40	149	1.29	ALL	Chemotherapy	14	35	32	21	18	17.24	14.78	40.2	34.4	1089	190	2			124711, 124712	LOW
58	SK	935269	8	F	17	121	0.76	ALL	Chemotherapy	6	30	25	24	19	10.84	8.58	18.3	14.5	854	180	2			124089, 123940	LOW
59	JK	1247624	15	F	42	149	1.32	ALL	Chemotherapy	6	14	13	8	7	6.94	6.07	16.6	14.5	983	160	2			124330, 124335	LOW
60	KB	941380	11	M	40	149	1.29	ALL	Chemotherapy	14	40	32	26	18	21.87	15.14	51.0	35.3	1122	170	2			124711, 124712	LOW
61	PA	1582896	4	F	13	196	0.84	ALL	Chemotherapy	10	35	29	25	19	10.84	8.24	12.6	9.5	900	200	2			137052, 136998	LOW
62	AP	1610837	7	M	20	119	0.81	AML	Chemotherapy	13	40	30	27	17	12.98	8.17	24.0	15.1	715	190	2			137053, 137063	LOW
63	GB	1553468	38	M	62	167	1.70	ALL	Chemotherapy	16	18	14	2	-2	2.19	-2.19	6.0	-6.0	769	180	2			135380, 135379	LOW
64	GG	1622194	15	F	46	150	1.38	AML	Chemotherapy	6	25	17	19	11	17.68	10.24	44.1	25.5	767	170	2			135663, 135661	LOW
65	MS	1403827	2	M	12	85.5	0.53	AML	Chemotherapy	14	36	30	22	16	6.60	4.80	11.1	8.1	915	200	2			135298, 135297	LOW
66	HK	1582606	12	F	30	150	1.12	ALL	Chemotherapy	12	42	31	30	19	23.29	14.75	46.9	29.7	875	160	2			130440, 130495	LOW
67	MC	72184	10	M	30	130	1.04	ALL	Chemotherapy	12	12	10	0	-2	0.00	-1.04	0.0	-2.3	915	200	2			130490, 130441	LOW
68	GS	1575462	14	M	69	152	1.71	ALL	Chemotherapy	16	38	35	22	19	24.82	21.43	75.2	65.0	834	170	2			129557, 129638	LOW
69	P	1331711	6	F	20	115	0.80	ALL	Chemotherapy	8	28	22	20	14	10.09	7.06	18.9	13.3	799	180	2			130443, 130579	LOW
70	SK	935269	8	F	17	123	0.76	ALL	Chemotherapy	6	26	25	20	19	8.19	7.78	13.7	13.0	987	190	2			124,089,123,940	LOW
71	HS	1418406	4	M	14.6	101	0.64	ALL	Chemotherapy	12	36	32	24	20	8.80	7.33	15.1	12.5	986	180	2			123,767,123,766	LOW
72	KB	941380	11	M	40	148	1.28	ALL	Chemotherapy	14	38	35	24	21	15.39	13.46	36.0	31.5	886	200	2			124,711,124,712	LOW

SR. NO.	NAME	MRD NO.	AGE	SEX	WEIGHT	HEIGHT	BSA	DIAGNOSIS	TREATMENT	PRE COUNT	POST COUNT 1 HR	POST COUNT 24 HR	PLT INCREMENT 1HR	PLT INCREMENT 24HR	CCI 1 HR	CCI 24 HR	PPR 1 HR	PPR24 HR	PLT COUNT OF PRODUCT/ UL	VOL OF PLT IN ML	No. of PLT transfused	SDP UNIT NO.	SDP DOSE	RDP UNIT NO.	RDP DOSE
73	JK	1247624	15	F	52	155	1.50	ALL	Chemotherapy	14	40	32	26	18	23.01	15.93	60.0	41.5	789	190	2			123454, 123456	LOW
74	SK	935269	8	F	25	128	0.94	ALL	Chemotherapy	16	40	32	24	16	12.96	8.64	25.8	17.2	976	180	2			123383, 123451	LOW
75	SD	863402	74	F	105	167	2.21	APLASTIC ANEMIA	Chemotherapy	10	35	28	25	18	31.91	22.98	113.9	82.0	987	190	2			115903, 115904	LOW
76	SD	863402	74	F	105	167	2.21	APLASTIC ANEMIA	Chemotherapy	10	60	52	50	42	28.74	24.14	102.5	86.1	950	400	4			115903,115904, 115912,115901	HIGH
77	SS	1276408	70	M	82	180	2.02	MULTIPLE MYELOMA	Chemotherapy	10	58	52	48	42	27.27	23.86	82.8	72.5	750	360	4			117264,1172301, 1172276,117306	HIGH
78	SSS	1276408	67	M	82	180	2.02	MULTIPLE MYELOMA	Chemotherapy	12	50	48	38	36	20.66	19.57	62.8	59.5	789	380	4			118901,118916, 118905,118911	HIGH
79	PK	1493133	39	F	65	160	1.70	AML	Chemotherapy	10	47	40	37	30	18.07	14.65	51.8	42.0	990	400	4			121861,121944, 121873,121915	HIGH
80	MC	72184	16	M	51	158	1.50	AML	Chemotherapy	12	66	54	54	42	25.50	19.83	65.2	50.7	850	360	4			136918,136913, 136909,136920	HIGH
81	SS	1199360	83	M	78	172	1.93	MDS	Chemotherapy	12	55	38	43	26	22.66	13.70	68.7	41.5	897	370	4			135443,135499, 135489,135490	HIGH
82	GG	1553468	38	M	62	162	1.67	ALL	Chemotherapy	14	42	28	28	14	12.56	6.28	35.0	17.5	876	380	4			135301,135299, 135270,135305	HIGH
83	HK	1402005	17	F	50	154	1.46	AML	Chemotherapy	6	57	46	51	40	19.63	15.39	50.3	39.5	865	400	4			135658,135688, 135690,135666	HIGH
84	JK	1247624	15	F	42	149	1.32	ALL	Chemotherapy	6	51	48	45	42	18.94	17.68	45.3	42.2	1015	360	4			124330,124333, 124338,124228	HIGH
85	SS	1276408	70	M	82	180	2.02	MULTIPLE MYELOMA	Chemotherapy	10	50	36	40	26	26.30	17.09	79.9	51.9	956	350	4			117264,117301, 1117276,117306	HIGH
86	GS	1575462	35	M	67	162	1.74	ALL	Chemotherapy	12	61	56	49	44	25.80	23.17	74.7	67.0	895	340	4			130011,130022, 130061,130064	HIGH
87	SK	1491085	20	F	60	180	1.73	ALL	Chemotherapy	12	55	53	43	41	22.57	21.52	58.6	55.9	999	330	4			118717,118802, 118885,118883	HIGH
88	JV	1553325	25	M	58	172	1.66	ALL	Chemotherapy	10	57	53	47	43	22.18	20.29	58.0	53.0	1212	360	4			131314,131333, 131356,131642	HIGH
89	SK	1491085	20	M	60	184	1.75	ALL	Chemotherapy	12	63	58	51	46	26.32	23.74	67.6	61.0	1209	390	4			118717,118802, 118805,118810	HIGH
90	K	1569877	42	M	67	158	1.71	ALL	Chemotherapy	12	61	57	49	45	22.34	20.51	65.5	60.1	984	380	4			131095,131098, 131102,131107	HIGH
91	JV	1535223	23	M	56	170	1.63	ALL	Chemotherapy	10	58	52	48	42	22.35	19.56	57.7	50.5	974	360	4			131101,131111, 131114,131116	HIGH
92	A	1580654	32	M	63	182	1.78	ALL	Chemotherapy	10	55	52	45	42	25.78	24.06	68.3	63.7	900	350	4			130063,130071, 130075,130080	HIGH
93	RC	433115	67	F	52	162	1.53	MULTIPLE MYELOMA	Chemotherapy	16	46	38	30	22	13.77	10.10	35.1	25.8	876	340	4			132061,132068, 132071,132074	HIGH
94	KS	1591382	15	M	50	154	1.46	ALL	Chemotherapy	13	55	50	42	37	18.80	16.56	48.2	42.5	888	330	4			136593,136601, 136605,13661O	HIGH
95	P	1618236	23	F	44	154	1.37	ALL	Chemotherapy	10	50	48	40	38	14.14	13.44	34.0	32.3	1023	400	4			136995,137002, 137009,137005	HIGH
96	KS	1591382	15	M	50	154	1.46	ALL	Chemotherapy	14	58	54	44	40	22.94	20.86	58.8	53.5	987	330	4			136909,136904, 136913,136906	HIGH
97	MC	72184	16	M	51	158	1.50	AML	Chemotherapy	15	42	38	27	23	13.27	11.30	33.9	28.9	887	350	4			139796,136802, 136810,136793	HIGH
98	K	1568678	32	M	70	185	1.90	ALL	Chemotherapy	12	45	38	33	26	17.74	13.98	49.1	38.7	887	360	4			131095,131098, 131102,131107	HIGH
99	GS	1575462	14	M	69	152	1.71	ALL	Chemotherapy	10	62	52	52	42	23.59	19.06	71.5	57.8	987	380	4			130628,130630, 130509,130610	HIGH
100	JK	1016336	85	M	78	170	1.92	AML	Chemotherapy	14	55	44	41	30	22.10	16.17	67.4	49.3	945	400	4			132618,132619, 132630,132641	HIGH

Baba Farid University
of Health Sciences
Sadiq Road
Faridkot-151 203 (Pb). INDIA.
Phone : 01639-256232,256236
Tele/Fax : 01639-256235
Email – Thesisbfuhs@gmail.com

No. BFUHS/2K23p-TH/ 3934

Date 14/03/2024

DAYANAND MEDICAL COLLEGE & HOSPITAL LUDHIANA
Receipt No. 3521
Date 18/3/24
Principal's Office

The Principal
Dayanand Medical College & Hospital
Ludhiana

Subject:: Approval of Plan of Thesis.

This is to inform you that the Faculty of Medical Sciences in its meeting held on 25.09.2023 has approved the plan of thesis of **Shalinderjeet Kaur**, a student of your college for **MD (Immuno Haematology & Blood Transfusion)** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
To analyze the response of platelet transfusion in onco hematology patients .

Supervisor
Dr. Sonia Gupta
Assoc. Professor
Dept. of I.H.B.T

Co-Supervisor
Dr. Rajesh Kumar
Professor & Head
Dept. of I.H.B.T

The student may submit the thesis in triplicate alongwith the plan in triplicate also, to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She may be directed to attach a photocopy of this letter with the forwarding letter while submitting thesis in the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic, if any.

Controller of Examinations

Note :

1. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*

All Concerned
18/3/2024

Scanned with CamScanner

Baba Farid University
of Health Sciences
Sadiq Road
Faridkot-151 203 (Pb). INDIA.
Phone : 01639-256232,256236
Tele/Fax : 01639-256235
Email – Thesisbfuhs@gmail.com

(32)

No. BFUHS/2K23p-TH/ 13220 **Date** 29/12/23

The Principal
Dayanand Medical College & Hospital
Ludhiana

Subject:: Approval of Plan of Thesis.

This is to inform you that the Faculty of Medical Sciences in its meeting held on 25.09.2023 has approved the plan of thesis of **Shalinderjeet Kaur**, a student of your college for **MD Immuno Haematology & Blood Transfusion** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
To analyze the response of platelet transfusion in onco hematology patients .

Supervisor
Dr. Sonia Gupta
Assoc. Professor
Dept. of I.H.B.T

Co-Supervisor-
Dr. Amarjit Kaur
Professor
Dept. of I.H.B.T

Co-Supervisor-
Dr. Rajesh Kumar
Professor
Dept. of I.H.B.T

The student may submit the thesis in triplicate alongwith the plan in triplicate also, to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She may be directed to attach a photocopy of this letter with the forwarding letter while submitting thesis in the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic, if any.

Controller of Examinations

Note :

1. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*

Scanned with CamScanner

TO ANALYZE THE RESPONSE OF PLATELET TRANSFUSION IN ONCOHEMATOLOGY PATIENTS

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED
IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MD

IN

IMMUNO HEMATOLOGY AND BLOOD TRANSFUSION
OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES
FARIDKOT

AUGUST, 2022

DR. SHALINDERJEET KAUR

DEPARTMENT OF IMMUNO HEMATOLOGY AND BLOOD TRANSFUSION
DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	To Analyze The Responseof Platelet Transfusion In Onco Hematology Patients
For the degree of	MD I.H.B.T
Name of the candidate	Dr. Shalinderjeet Kaur
Supervisor	Dr. Sonia Gupta, Associate Professor, Department of I.H.B.T, Dayanand Medical College and Hospital
Co-supervisor	Dr. Amarjit Kaur, Professor & Head, Department Of I.H.B.T, Dayanand Medical College and Hospital Dr. Rajesh Kumar, Professor, Department of I.H.B.T, Dayanand Medical College and Hospital
Institution	Dayanand Medical College & Hospital, Ludhiana
University	Baba Farid University Of Health Sciences, Faridkot

Introduction: Disease and therapy related hypo proliferative thrombocytopenia is a major problem when managing patients with hematological malignancies and massive platelet transfusions are often required to reduce the risk of hemorrhage. Platelet transfusion refractoriness is encountered in up to 30% of patients having hematological disease.

Aim of study: To study the response of low and high dose of platelet transfusion in onco hematological patients.

Material and method: Study population will include 100 patients who have an adequate platelet response and are unlikely to be refractory to platelet transfusion at the time of enrollment and would require multiple platelet transfusion. Single donor apheresis platelets (SDAPs) will be prepared by using, automated cell separator and pooled platelet concentrate will be prepared from whole blood donation, low dose, apheresis product will be split, using sterile connecting connecting device into two low dose products (i.e. $1.5X10^{11}$platelet/unit). Pooled platelet concentrate of two units 1-1.5-$X10^{11}$ or four platelet concentrate units of 2.5- $3X10^{11}$.

The post transfusion counts will be assessed after one hour and 24h of transfusion and corrected count increment (CCI), percent platelet recovery (PPR) will be calculated.

Clinical significance: Platelet transfusion is an integral part of modern oncological practice and is used to treat hemorrhage associated with thrombocytopenia. We well assess the role of low and high dose of platelet transfusion in these patients.

Keywords: Platelet refractoriness, onco heamatology, single donor aphersesis, corrected count increment, percent platelet recovery.

(Signature) Candidate	(Signature) Supervisor	(Signature) Co-supervisor	(Signature) Co- supervisor	(Signature) Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"TO ANALYZE THE RESPONSEOF PLATELET TRANSFUSION IN ONCO HEMATOLOGY PATIENTS"** exist in the Department of Immuno hematology and Blood Transfusion at DMC&H, Ludhiana and will be provided to be candidate of will be provided to the candidate. We will see that the data being included in the thesis are genuine and is collected by the candidate herself under our supervision and guidance.

Supervisor

Sonia Gupta
Dr. Sonia Gupta
Associate Professor
Department of I.H.B.T
DMCH, Ludhiana

Co-Supervisors

Amarjit
Dr. Amarjit Kaur
Professor and Head
Department of I.H.B.T
DMCH, Ludhiana

Dr. Rajesh Kumar
Professor
Department of I.H.B.T
DMCH, Ludhiana

Head of the Department

Amarjit
Dr. Amarjit Kaur
Professor and Head
Department of I.H.B.T
DMCH, Ludhiana

Place: Ludhiana

Date: 30/09/22

APPROVAL PROFORMA
BY RESEARCH & ETHICAL COMMITTEE
DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

Name of candidate	Dr. Shalinderjeet Kaur
Department	I.H.B.T
Topic of Thesis	TO ANALYZE THE RESPONSEOF PLATELET TRANSFUSION IN ONCO HEMATOLOGY PATIENTS
Likely date of appearing in PG examination	May/June, 2024
Date of enrollment	04th April, 2022
Name of Head of Department	Dr. Amarjit Kaur
1. Supervisor **2. Co-Supervisor**	Dr. Sonia Gupta Dr. Amarjit Kaur Dr. Rajesh Kumar
Signature of Members of Research Committee with Stamp	**Signature of Members of Ethics Committee with Stamp**
Dr. Harpreet Kaur (Professor & Head, Pathology)	Mr. R K Sharma (Legal Expert)
Dr. Jaspal Singh (Professor & Head, Surgery)	Dr. Ramit Mahajan (Associate Professor, Gastroenterology)
Dr. Dinesh Gupta (Professor & Head, Medicine)	Dr. Anu Sharma (Professor, Anatomy)
Dr. Sandeep Kaushal (Dean Academics & Professor & Head, Pharmacology)	Dr. Sandeep Kaushal (Dean Academics & Professor & Head, Pharmacology)
Dr. Gurpreet S Wander (Vice Principal)	Dr. Gurpreet S Wander (Vice Principal & Professor & Head, Cardiology)
	Dr. Gagandeep Singh (Secretary, Ethics Committee Professor & Head, Neurology)

Approved: Yes / ~~No~~

Dr. Sandeep Puri
Chairperson
Research Committee

Chairperson
Research Committee

Approved: Yes / ~~No~~

Prof. Arvind Malhotra
Chairperson
Ethics Committee

Chairperson
Ethics Committee

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

1	NAME OF THE CANDIDATE AND ADDRESS	DR. SHALINDERJEET KAUR
2	NAME OF THE INSTITUTE	DAYANAND MEDICAL COLLEGE AND HOSPITAL, LUDHIANA
3	COURSE OF STUDY AND SUBJECT	MD IMMUNO HEMATOLOGY AND BLOOD TRANSFUSION
4	DATE OF ADMISSION OF COURSE	04/04/2022
5	TITLE OF THE TOPIC	TO ANALYZE THE RESPONSE OF PLATELET TRANSFUSION IN ONCOHEMATOLOGY PATIENTS

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Platelet transfusion is highly effective therapy for hemorrhage in severely thrombocytopenic patients and is an integral part of modern oncologic therapeutic practice. Recent surveys documents a steadily increasing usage of platelet in india with an increasing proportion of single donor apheresis (SDP) products opposed to pooled Random donor platelets (RDP).[1] Platelet transfusion refractoriness (PTR) can be caused by immunological and non immunological factors with non immunological factors responsible for 60% to 80% of cases. . Immunonological factors plays a role in 10% to 25% of patients include antibodies against four antigen classes HLA class 1 , human platelet antigen (HPA), ABO and drug dependent antibodies.[2]

A study showed that leucoreduction lowered HLA alloimmunization from 19% to 7% and alloimmune platelet refractoriness from 14% to 4% for patients undergoing chemotherapy haemat-oncology patients[2]. PTR includes immune and non immune factors . non immune factors include fever, severe infection, splenomegaly , disseminated intravascular coagulation (DIC) and the use of antibiotics.[3]

Among the immune factors , humoral immunity is currently considered to be the main reason including ABO blood group incompatibility , HLA antigen incompatibility and antibodies produced by platelet specific antigens (HPA). Leukocyte reduction removes more than 90% of white blood cells and can delay or prevent the onset of ineffective platelet transfusion caused by the development of HLA antibodies.

In general there is a lack of ineffective method to completely prevent and treat immunological PTR and the occurrence of PTR is still a huge challenge for clinicians. A threshold of $10X10^9$/l platelet transfusion should be utilized in adults receiving therapy for haemato-oncology patients

Acute myeloid leukemia patients with multiple platelet transfusion some patients never develop immunological PTR while some patients are more prone to allogenic immunity and lead to PTR. Most studies have shown that for patients with hematological diseases injection of high dose gamma globulin, plasma exchange and rituximab therapy can improve PTR to a certain extend HLA antibodies are significantly lower than before immunotherapy.. PTR often occurs in patients with acute leukemia which increases the risk of bleeding PTR further aggravates the demand for platelets and aggravates the limited availability of platelet supply. In acute myeloid leukemia (AML) patients with multiple platelet transfusion , some patients never develop immunological PTR while some patients are more prone to allogenic immunity and lead to PTR , there was no difference in age and gender of patients between these two groups. In AML it is found that PTR is more likely to occur in patients with a history of pregnancy, extramedullary infilteration , low white blood cell count, infection and hemophagocytic syndrome. The early and late mortality due to severe bleeding was significantly higher in patients with PTR than in patients without PTR.

6.2 REVIEW OF LITERATURE

Onco-hematological disease induces thrombocytopenia and hemorrhagic manifestation as a result of bone marrow failure caused by the disease itself and/or by the type of treatment used (radiotherapy and /or chemotherapy) . In these cases platelet transfusion is the main therapy used for the prevention and treatment of hemorrhagic manifestation.[4] Platelet refractoriness is a result of shortened survival of platelets brought about by factors of immunological and or non immunological factors.[5] Since platelets were first identified in 1881, there has been continuous and accelerating progress in our basic understanding of platelet function. Platelets are anucleated, discoid cell, roughly 2-3 um in diameter that function primarily as regulators of hemostasis, but also play secondary roles in angiogenesis and innate immunity.although human adults contain nearly one trillion platelets in circulation that are turned over every 8-10 days. Platelets stem from large (30-100um)nucleated cells called megakaryocytes that resides primarily in in the bone marrow. During maturation megakaryocytes extend long proplatelet elongations into sinusoidal blood vessles from which platelets ultimately release. During this process, platelets develop a number of distinguishable structural elements, including a delimited plasma membrane, invagination of plasma membrane that form the open canalicular system (OCS), a closed channel network of residual endoplasmic reticulum that forms a dense tubular system (DTS), a spectrin based membrane skeleton, an actin based cytoskeletal network, a peripheral band of microtubules, and numerous organelles including alpha granules, dense granules, peroxisomes, lysosomes, and mitochondria. The approximately 1 trillion platelets that circulate in an adult human are small anucleated cell fragments adapted to adhere to damaged vessels, to aggregate with one another, and to facilitates the generation of thrombin. These actions contribute to hemostasis by producing platelet plug, and then reinforcing plug strength by action of thrombin converting fibrinogen to fibrin strands to accomplish

these tasks, platelets have surface receptors that can bind adhesive glycoprotein, these include the GP1b/9/5 complex, which supports platelet adhesion by binding von willebrand factor esp under conditions of high shear, and the alpha2bb3 (GP2b/3a) receptors,which is platelet specific and mediates platelet aggregation by binding fibrinogen and/or von willebrand factor. Activated platelets express both surface P selectin, which mediates interaction with leukocytes,and CD40ligand, which activates a number of proinflammatory cells, and release chemokines and a soluble form of CD40 ligand, thus initiating an inflammatory reaction. Platelet coagulant activity results from the exposure of negatively charged phospholipids on the the surface of platelets and the generation of platelet microparticles, along with release of specific receptors for activated coagulation factors. Platelets acts as storehouse for a variety of molecules that affects platelet function, inflammation, innate immunity, cell proliferation, vascular tone, fibrinolysis, and wound healing; these agents are actively released upon platelet activation. Other vasoactive and platelet activating substances are newly synthesized when platelets are activated. Platelets play a central role in hemostasis by initiating and propagating thrombus, and as a physical constitutent of the resulting clot. In vitro measures of platelet number and agonist- induced aggregation are relatively poor predictors of hemorrhage, as platelet function in vivo is influenced by a complex milieu, affected by metabolic aberrations (e.g. sepsis, uremia) local vascular defects and coagulation factor deficiencies. Routine clinical assessment of platelet function in vivo is limited to bleeding time (BT) assay, first described by Duke in 1910. Harker and Slichter showed that the BT in patients with thrombocytopenia due to decreased platelet production, is relatively unaffected at platelet counts above $100X10^9$/l. It is prolonged in a linear fashion as counts fall to $10X10^9$/l. At counts of $<10X10^9$/l, the BT is >30 min and not related to platelet count. These data provide a rationale for the present practice of transfusing platelets to a threshold of $>50X10^9$/l in surgical patients and

those with active bleeding. The biological basis for the prophylactic use of platelets is more difficult to define. In, in vivo studies, Hanson and slichter found that platelet survival was moderately reduced when the counts were 50- 100X10^9/l, but were markedly reduced at counts of <50X10^9/l. these data were explained by two phase model based on a predicted maximal platelet lifespan of 10.5 days and daily platelet loss due to senescence(10-15% per day) plus a secondary consumption of approximately 7.1X10^9/l platelets per day required for the maintenance of 'vascular endothelial integrity'. Quantitative and qualitative disorders of platelet produce hemorrhagic diatheses. On pathological states, uncontrolled platelet thrombus formation can lead to vasoocclusion and ischemic tissue necrosis. Despite this relatively small size platelets play essential role in the maintenance of hemostasis. The first successful attempt to raise the platelet count in thrombocytopenic patients by transfusion of whole blood was described by duke in 1910. Two types of platelet concentrate are available for transfusion; one which is the Random donor platelet (RDP) include platelet rich plasma concentrate (PRP-PC), buffy coat platelet concentrate (BC-PC) and second is Single voluntary thrombocytoapheresis donors with the help of an automated cell separator.[6] Platelet transfusion are the primary therapy for thrombocytopenia due to various causes. Superiority of SDP over RDP transfusion is largely assumed, but not unproven. Now a day, there has been an increasing trend towards using SDP by Apheresis as an alternative to pooled RDP for platelet transfusion therapy.the use of SDP is preferred over RDP as it represents fewer donor exposure and, therefore, lowers risk of transmission of virus, alloimmunization, and transfusion associated septic reactions and "better" platelet quality.[7] In this study Ethylenediaminetetraaceticacid (EDTA) anticoagulated blood sample were collected for platelet count before transfusion and 1 hour after transfusion from each patient.[8] The response to transfusion was

evaluated by calculating the corrected count increament (CCI) one hour after transfusion as follow

$$CCI = \frac{\text{(platelet increment /ul)X(body surface area in } m^2\text{)X10\^11}}{\text{Number of platelet transfused}} = \text{platelets/ul/}m^2$$

All counts were performed normally after dilution with ammonium oxalate. Platelet are considered be refractory when they presented two successive counts of post transfusion platelet increment of less than 5000[4].

$$PPR = \frac{\text{[(platelet concentrate/ul)x(weight in kg x75 ml)]x100}}{\text{Platelet count of products/ul X volume of platelet in ml}} = \text{platelet count \%}$$

Platelet transfusion is highly effective therapy for hemorrhage in severely thromobocytopenic patients and is an integral part of modern oncological therapeutic practice. It may be reasonably argued that bone marrow and stem cell transplantation would not be feasible without the prior development of effective means of treating and preventing hemorrhage in severely myelosuppressed and thrombocytopenic patients. Recent surveys document a steadily increasing usage of platelets in USA as many as1.3 million doses in 1994 with a increasing proportion of single donor platelets (SDP) products as opposed to pooled random platelets. A national cancer institute study from 1954 to 1963 showed that the major cause of death in 52% of 414 acute leukemia patients was hemorrhage. By the 1980s when platelet transfusion were available and commonplace, the percentage of adults with acute lymphoblastic leukemia with lethal hemorrhagic complications had dropped to only 3%.[9] Studies performed in 1970s and 1980s showed that prophylactic transfusion decrease the incidence of significant bleeding episodes in leukemia patients but failed to

demonstrate a longer survival in those transfused patients transfused prophylactically as opposed to those transfused only in the presence of bleeding.[10-12] Most studies of prophylactic use of platelet advocated <20X10^9/l as the appropriate threshold for transfusion. This was usually based on the 1962 publication by Gaydos et.al.[13] In contrast, Gmur et al.[14] found that the reduction in donor exposure with the use of SDP resulted in reduced alloimmunization. Patients receiving SDP became refractory less frequently after a longer period of time and after a higher no. of transfusion than those receiving pooled RDP. The study concluded that the use of SDP postpone alloimmunization possible explanation for these differing results include the lower average no. of donor exposure. A single platelet concentrate containing approximately 3X10^{11} platelets is expected to raise platelet count by 30,000-60,000/ul while the RDP containing approximately 7X10^{10} platelets increases the platelet count by 5,000-10,000/ul in an average sized adults. Most institutions adopted policies for “standard”platelet dose to give one platelet concentrate 10kg of body weight and this should increase the platelet count by approximately 40,000/ul.[15] In study patients that developed PTR during induction chemotherapy platelets count was measured daily and transfusion of ABO identical platelet from apheresis products or pooled platelet (0.5-1.0X10^{11} platelet per 10kg) was performed to patients with a platelet count <10X10^9/l to patient with an active bleeding to patients with platelet count <20X10^9/l and fever >38^{oc}.[16] Platelet count one hour after the end of transfusion and subsequent formulae to asses transfusion refractoriness are not in routine practice. Therefore a clinical definition is used i.e. persistent thrombocytopenia <10X10^9/l despite at least two successive daily platelet transfusion to define PTR. Finding a compatible platelet unit for an alloimmunized patient depends on the tests available,the frequency of the patient’s HLA type relative to the pool of HLA matched donors and the level of alloimmunization. Platelet crossmatching and HLA matching are frequently uses , the success rate of

these strategies is comparable.[17-19] Platelet crossmatch method is usually the fastest and easiest way to obtain a compatible unit. The solid phase red cell adherence assay mixes a panel of donor platelets with the patient's serum. Antibodies against HLA and HPA that bind to the platelets are visualized with indicator red cell coated with anti-immunoglobin G. The crossmatch approach is commonly used because compatible units usually can be obtained within 24 hours, and both HLA and HPA compatibility issues are covered with no additional testing. Despite these advantages, HLA matched platelets may reduce future alloimmunization. Most importantly, platelet crossmatching tends to be problematic with highly alloimmunized patients, which can make it difficult to find enough compatible units .Patients with platelet refractoriness can be supported with apheresis platelets from donor whose HLA-A and HLA-B antigens match those of the patient. However, obtaining a supply of 4/4 matches is possible only for blood centers that have a large no. of HLA typed donors and a well organized inventory. Blood centers that cannot track the HLA type of units in the inventory must resort to recruiting known donors, which causes delay in obtaining units and usually allows a very limited supply of platelet units. When exact matches unavailable, one can use the antibody profile determined by the single antigen bead test to select donor units that lack the corresponding cognate antigens (i.e. HLA compatible).[20-22] This antibody specificity prediction (ASP) method is equivalent to HLA matching in terms of efficacy. In addition, the ASP method increases the pool of compatible donors when compared with the number available under traditional HLA matching criteria, making it easier to support patients with platelet refractoriness.[22] It is important to note that an HLA compatible units carries a potential risk for further alloimmunization, similar to a crossmatch - compatible unit. Although the incidence of HPA antibodies causing transfusion refractoriness is small, this possibility should be investigated when most of the crossmatches are incompatible or when HLA matched transfusions fail. If antibodies against

HPA are present, then donor of known platelet antigen phenotype may be recruited.[22]

6.3 AIMS AND OBJECTIVES OF THE STUDY

- To study the response of low and high dose of platelet transfusion in onco hematological patients.

7. MATERIALS AND METHODS

Study population will include 100 patients who have an adequate platelet response and are unlikely to be refractory to platelet transfusion at the time of enrollment and would require multiple platelet transfusion.

ABO identical single donor apheresis platelets (SDAPs) will be prepared by using, automated cell separator (Trima, Haemonetics)and pooled platelet concentrate will be prepared from whole blood donation collected from voluntary donors who qualified the criteria for apheresis platelet donation and whole blood donation as per Directorate General of Health services (DGHS) technical manual. For standard dose, platelet yield of 3X1011/unit was harvested. For low dose, apheresis product was split, using sterile connecting connecting device into two low dose products (i.e. 1.5X1011platelet/unit). Pooled platelet concentrate of two units 1-1.5X1011 or four platelet concentrate units of 2.5 -3 X1011

Samples of the platelet concentrate (PC) will be obtained from the segment tube of the bag in the sterile conditions for the platelet count.

Volume of product = weight of the product/ specific gravity

Ethydiaminetetraacetic acid (EDTA) anticoagulated blood samples will be collected for platelet count before transfusion. The post transfusion counts will be assessed after one hour and 24h of transfusion and corrected count increment (CCI), percent platelet recovery (PPR)will be calculated.

Samples of the platelet concentrate (PC) will be obtained from the segment tube of the bag in the sterile conditions for the platelet count component

Evaluation of the response to platelet transfusion-

The response to transfusion will be calculated by corrected count increment (CCI) one hour after transfusion as follows;

$$CCI = \frac{\text{(platelet increment /ul)X(body surface area in } m^2\text{)X10\^11}}{\text{Number of platelet transfused}} = \text{platelets/ul/}m^2$$

$$PPR = \frac{\text{[(platelet concentrate/ul)x(weight in kg x75 ml)]x100}}{\text{Platelet count of products/ul X volume of platelet in ml}} = \text{platelet count \%}$$

Platelet increment =post platelet transfusion count –pre transfusion count

Estimation of body surface area= $\sqrt{\frac{\text{height(cm)xweight (kg)}}{60}}$

7.1 SOURCE OF DATA

The study will be conducted in the Immuno hematology and Blood Transfusion & Oncology department of Dayanand medical college and hospital.

7.2 METHOD OF COLLECTION OF DATA

Inclusion criteria-

- Patients without any active bleeding at the time of enrolment.
- Thrombocytopenic hemato-oncology patients and patients on chemotherapy for hemato oncological malignancies which are non refractory to platelet transfusion.

Exclusion criteria-

- Bleeding during study period
- Use of drugs affecting platelet number function (eg. Amphotericin B , vancomycin)
- Thrombotic thrombocytopenic purpura (TTP)
- Hemolytic uremic syndrome (HUS)
- Fever or sepsis
- Patients with splenomegaly and splenectomy

Outcome: Platelet transfusion is an integral part of modern oncological practice and is used to treat hemorrhage associated with thrombocytopenia. Improved knowledge on the mechanism of the immune and non-immune causes of Platelet Transfusion Refractoriness (PTR) are needed to design a rational therapeutic strategy that aims to improve the efficiency of transfusion.

Statistical: Data will be described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. To determine whether the data is normally distributed, a Kolmogorov-Smirnov test will be used. Comparison of quantitative variables will be done using Paired t-test and Wilcoxon rank test for independent samples for parametric and non-parametric data respectively. A probability value (p value) less than 0.05 will be considered statistically significant. All statistical calculations will be done using (Statistical Package for the Social Science) SPSS 21version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

No

7.4 HAS ETHICAL CLEARENCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Yes, Attached herewith.

8. LIST OF REFERENCES

1. Wallace EL, Churchill WH, Surgenor DM, Cho GS, Mc Gurk S. collection and transfusion of blood and blood components in the united states. Transfusion 1998;38:625-36
2. Cohn CS. Platelet transfusion refractoriness: how do I diagnose and manage?. Hematology 2014, the American Society of Hematology Education Program Book. 2020;2020:527-32.
3. Ueno H, Klechevsky E, Morita R, et al. Dendritic cell subsets in health and disease. Immunol Rev 2007;219:118-42.
4. Ferreira AA, Zulli R, Soares S, Castro VD, Moraes-Souza H. Identification of platelet refractoriness in oncohematologic patients. Clinics. 2011;66:35-40.
5. Slichter SJ, Davis K, Enright H, Braine H, Gernsheimer T, Kao K, et al. Factors affecting post-transfusion platelet increments, platelet refractoriness, and platelet transfusion intervals in thrombocytopenic patients. Blood. 2005;105:4106–14. 10.1182/blood-2003-08-2724
6. Slichter SJ. Platelet transfusion therapy. Hematol Oncol Clin North Am. 1990;4:291-311.
7. Wallace EL, Churchill WH, Surgenor DM. Collection and transfusion of blood and blood components in the United States, 1992. Transfus. 1995;35:802-12.
8. Legler TJ, Fischer I, Dittmann J, Simson G, Lynen R, Humpe A, et al. Frequency and causes of refractoriness in multiply transfused patients. Annals of Hematology. 1997;74:185 189. 10.1007/s002770 050280
9. Benjamin RJ, Anderson KC. What is the proper threshold for platelet transfusion in patients with chemotherapy induced thrombocytopeni a? Critical reviews in oncology/hematology. 2002;42:163-71.
10. Higby DJ, Cohen E, Hollanf JF, Sinks L. the prophylactic treatment of thrombocytopenic leukemic patients with paltelets; a double blind study. Transfusion 1974;14:440-6

11. Roy AJ, Jaffe N, Djerassi I. prophylactic platelet transfusion in children with acute leukemia: a dose response study. Transfusion 1973;13:283-90.
12. Murphy S, Litwin S, Herring LM, et.al. indication for platelet transfusion in children with acute leukemia. Am J Hematol 1982;12;347-56.
13. Gaydos LA, Freireich EJ, mantel N. The quantitative relation between platelet count and hemorrhage in patients with acute leukemia. New Engl J Med 1962;66:178-88.
14. Gmur J, von Felten A, osterwalder B, et.al. delayed alloimmunization using random single platelet transfusion: identification of a large group of patients who do not become alloimmunized. Blood 1981;58:1007-11.
15. O'Connel B, Lee EJ Schiffer CA. the value of 10 minutes post transfusion paltelets counts. Transfusion 1998;28:66-7.
16. Haute Autorite de santé , transfusion De Plaquettes; Produites indications; recommendations De Bonne Pratique Clinique,(2015).
17. Moroff G, Garraty G, Heal JM, et al. selection of platelets for refractory patients by HLA matching and prospective crossmatching. Transfusion 1992;32:633-640.
18. Rioux- Masse B, Cohn C, Lindgren B, Pulkrabek S, McCullough J. utilization of cross matched or HLA matched platelets for patients refractory to platelet transfusion. Transfusion. 2014;54:3080-87.
19. Seike K, Fujii N, Asano N, Ohkuma S, Hirata Y, Fujii K et al. Efficacy of HLA virtual cross-matched platelet transfusions for platelet transfusion refractoriness in hematopoietic stem cell transplantation. Transfusion. 2020;60:473-8.
20. Hod E, schwartz J. platelet transfusion refractoriness. Br J Haematal. 2008;142:348-60.

21. Vasallo RR Jr. new paradigms in the management of alloimmune refractoriness to platelet transfusion. Curr Opin Hematol .2007;14:655-63.
22. Petz LD, Garratty G, Calhoun L, Clark BD, Terasaki PI, Gresens C, et al. Selecting donors of platelets for refractory patientson the basis of HLA antibody specificity. Transfusion. 2000;40:1446-56.

PROFORMA

Sr. No.

Name of the patient:

Age/Sex:

Weight/Height:

MRD No:

Diagnosis:

Treatment:

Pre transfusion platelet count of patient

Post transfusion platelet count of patient- 1 hr

24 hr

Corrected count increment (CCI)- 1 hr

24 hr

Percent platelet recovery (PPR) -1 hr

24 hr

SDP unit no.--

SDP dose – Low

Standard dose

Pooled platelet concentrate unit no.--

Pooled platelet concentrate—2 units dose

4 units (Standard dose)

Signature of Candidate **Signature of Supervisor**

INFORMED PATIENT CONSENT

Date: _____

I……..D/o,W/o,S/o…… ……. ……am willing to participate in the study **"TO ANALYZE THE RESPONSE OF PLATELET TRANSFUSION IN ONCOHEMATOLOGY PATIENTS"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

……	……
Signature of the Witness	Signature of the patient
Name:	

Signature of Candidate **Signature of Supervisor**

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____

निवासी _____ इस शोधकार्य **"TO ANALYZE THE RESPONSE OF PLATELET TRANSFUSION IN ONCOHEMATOLOGY PATIENTS"** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____ _____

गवाह के हस्ताक्षर रोगी के हस्ताक्षर/अंगूठे का निशान

नाम: नाम:

_____

अन्वेषक केहस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

<u>ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ</u>

ਮਿਤੀ_____

ਮੈ_____ ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____ ਵਾਸੀ _____ **“TO ANALYZE THE RESPONSE OF PLATELET TRANSFUSION IN ONCOHEMATOLOGY PATIENTS”** ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾਮਨੇਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ–ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

_____

ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ